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********** STN Columbus **********
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FILE 'HOME' ENTERED AT 15:12:44 ON 18 OCT 1999

=> file medline
COST IN U.S. DOLLARS                SINCE FILE     TOTAL
                                    ENTRY   SESSION
FULL ESTIMATED COST                   0.27      0.27

FILE 'MEDLINE' ENTERED AT 15:12:49 ON 18 OCT 1999

 FILE LAST UPDATED: 14 OCT 1999 (19991014/UP). FILE
COVERS 1960 TO DATE.

 MEDLINE has been reloaded to reflect the annual MeSH changes
made by
 the National Library of Medicine for 1999. Enter HELP RLOAD for
details.

 OLDMEDLINE, data from 1960 through 1965 from the Cumulated
Index
 Medicus (CIM), has been added to MEDLINE. See HELP
CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in
the
 Basic Index. See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY
AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> s stroma#(p)(exogenous gene or gene construct or vector)/ab,bi
'AB' IS NOT A VALID FIELD CODE
      26070 STROMA#
          0 EXOGENOUS GENE/AB
      52796 EXOGENOUS/BI
     418026 GENE/BI
        140 EXOGENOUS GENE/BI
            ((EXOGENOUS(W)GENE)/BI)
          0 GENE CONSTRUCT/AB
     418026 GENE/BI
      18002 CONSTRUCT/BI
        626 GENE CONSTRUCT/BI
            ((GENE(W)CONSTRUCT)/BI)
          0 VECTOR/AB
      32375 VECTOR/BI
L1       142 STROMA#(P)(EXOGENOUS GENE OR GENE
CONSTRUCT OR VECTOR)/AB,BI

=> s l1 and promoter#/ab,bi
'AB' IS NOT A VALID FIELD CODE
          0 PROMOTER#/AB
      68078 PROMOTER#/BI
L2        26 L1 AND PROMOTER#/AB,BI

=> s l2 and collagen/ab,bi
'AB' IS NOT A VALID FIELD CODE
          0 COLLAGEN/AB
      72799 COLLAGEN/BI
L3         1 L2 AND COLLAGEN/AB,BI

=> d

L3  ANSWER 1 OF 1  MEDLINE
AN  1998281597    MEDLINE
DN  98281597
TI  Construction of temperature and Zn-dependent human stromal cell
lines that
    amplify hematopoietic precursors from cord blood CD34+ cells.
AU  Gauthier L; Fougereau M; Tonnelle C
CS  Centre d'Immunologie INSERM-CNRS de Marseille-Luminy,
France.
SO  EXPERIMENTAL HEMATOLOGY, (1998 Jun) 26 (6) 534-40.
    Journal code: EPR. ISSN: 0301-472X.
CY  United States
DT  Journal; Article; (JOURNAL ARTICLE)
LA  English
FS  Priority Journals; Cancer Journals
EM  199808
EW  19980804


=> d ab

L3  ANSWER 1 OF 1  MEDLINE
AB  Forty-five human  ***stromal***  cell lines were established
from
    long-term bone marrow cultures transformed with a new
***vector*** ,
    pNu MTSVts, which contains the Zn-inducible metallothionein
     ***promoter***  and the temperature-dependent SV40 T antigen
from SV40
    A58 mutant. Six of these cell lines were studied because of their
growth
    capacity. All cell lines differed with respect to growth potential,
    expression of cell surface markers, and cytokine transcripts. Major
    histocompatibility complex (MHC) class I, CD29, CD49d, and
CD51 were
    present on all  ***stromal***  cell lines, MHC class II and CD34
were
    consistently absent, and CD11a (LFA-1), CD18 (ICAM-1R), CD54
(ICAM-1),
    CD58 (LFA-3) CD56 (N-CAM), CD106 (V-CAM), laminin, and
***collagen***
    IV were diversely expressed. All cell lines contained interleukin
    (IL)-1alpha, IL-1beta, IL-2, IL-5, and macrophage
colony-stimulating
    factor (M-CSF) transcripts, whereas granulocyte M-CSF,
TNFalpha, IL-3,
    IL-4, and IL-7 were diversely expressed. The most characteristic
feature
    of these cells was their varying capacity to expand cord blood
CD34+
    cells. One of these  ***stromal***  cell lines ensured more than
twofold
    expansion of the initial CD34+CD10-CD19- population in the first
2 weeks.
    Differentiation toward the B cell lineage was limited, producing
only very
    small numbers of CD19+ cells after 6 weeks of culture.


=> s mesenchym?/ab,bi
'AB' IS NOT A VALID FIELD CODE
          0 MESENCHYM?/AB
      14675 MESENCHYM?/BI
L4    14675 MESENCHYM?/AB,BI

=> s l4(p)(gene construct or exogenous gene or vector#)/ab,bi
'AB' IS NOT A VALID FIELD CODE
          0 GENE CONSTRUCT/AB
     418026 GENE/BI
      18002 CONSTRUCT/BI
        626 GENE CONSTRUCT/BI
            ((GENE(W)CONSTRUCT)/BI)
          0 EXOGENOUS GENE/AB
      52796 EXOGENOUS/BI
     418026 GENE/BI
        140 EXOGENOUS GENE/BI
            ((EXOGENOUS(W)GENE)/BI)
          0 VECTOR#/AB
      60999 VECTOR#/BI
L5        64 L4(P)(GENE CONSTRUCT OR EXOGENOUS GENE
OR VECTOR#)/AB,BI

=> s l5 and promoter#/ab,bi
'AB' IS NOT A VALID FIELD CODE
          0 PROMOTER#/AB
      68078 PROMOTER#/BI
L6        12 L5 AND PROMOTER#/AB,BI

=> d l- bib ab
YOU HAVE REQUESTED DATA FROM 12 ANSWERS -
CONTINUE? Y/(N):y

L6  ANSWER 1 OF 12  MEDLINE
AN  1999257883    MEDLINE
DN  99257883
TI  Expression of human bone morphogenic protein 7 in primary
rabbit
    periosteal cells: potential utility in gene therapy for osteochondral
    repair.
AU  Mason J M; Grande D A; Barcia M; Grant R; Pergolizzi R G;
Breitbart A S
CS  Department of Research, North Shore University Hospital-New
York
    University School of Medicine, Manhasset, USA.
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SO GENE THERAPY, (1998 Aug) 5 (8) 1098-104.
Journal code: CCE. ISSN: 0969-7128.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
EW 19990801
AB A commonly encountered problem in orthopedics is bone and cartilage tissue
injury which heals incompletely or without full structural integrity. This
necessitates development of improved methods for treatment of injuries
which are not amenable to treatment using current therapies. An already
large and growing number of growth factors which play significant roles in
bone remodeling and repair have been identified in the past few years. It
is well established that bone morphogenic proteins induce the production
of new bone and cartilage. An efficient method of delivery of these growth
factors by conventional pharmacological means has yet to be elucidated. We
wished to evaluate the use of retroviral ***vector*** -mediated gene
transfer to deliver genes of therapeutic relevance for bone and cartilage
repair. To determine the feasibility of using amphotropically packaged
retroviral ***vectors*** to transduce primary rabbit
mesenchymal stem cells of periosteal origin, primary periosteal
cells were isolated from New Zealand white rabbits, transduced in vitro
with a retroviral ***vector*** bearing both the nuclear localized lacZ
marker gene and the neo(r) gene, and selected in G418. We used a
convenient model for analysis of in vivo stability of these cells which
were seeded on to polymer scaffold grafts and implanted into rabbit
femoral osteochondral defects. The nuclear localized beta-galactosidase
protein was expressed in essentially 100% of selected cells in vitro and
was observed in the experimental explants from animals after both 4 and 8
weeks in vivo, while cells transduced with a retroviral ***vector***
bearing only the neo(r) gene in negative control explants showed no blue
staining. We extended our study by delivering a gene of therapeutic
relevance, human bone morphogenic protein 7 (hBMP-7), to primary
periosteal cells via retroviral ***vector*** . The hBMP-7 gene was
cloned from human kidney 293 cell total RNA by RT-PCR into a retroviral
vector under control of the CMV enhancer/ ***promoter*** .
Hydroxyapatite secretion, presumably caused by overexpression of hBMP-7,
was observed on the surface of the transduced and selected periosteal
cells, however, this level of expression was toxic to both PA317 producer
and primary periosteal cells. Subsequently, the strong CMV enhancer/
promoter driving the hBMP-7 gene was replaced in the retroviral
vector by a weaker enhancer/ ***promoter*** from the rat
beta-actin gene. Nontoxic levels of expression of hBMP-7 were confirmed at
both the RNA and protein levels in PA317 producer and primary periosteal
cell lines and cell supernatants. This work demonstrates the feasibility
of using a gene therapy approach in attempts to promote bone and cartilage
tissue repair using gene-modified periosteal cells on grafts.

L6 ANSWER 2 OF 12 MEDLINE
AN 1999230327 MEDLINE
DN 99230327
TI Transforming growth factor-beta1 induces interleukin-6 expression via
activating protein-1 consisting of JunD homodimers in primary human lung
fibroblasts.
AU Eickelberg O; Pansky A; Mussmann R; Bihl M; Tamm M; Hildebrand P;
Perruchoud A P; Roth M
CS Department of Research and Internal Medicine, University Hospital, 4031
Basel, Switzerland.. oliver.eickelberg@yale.edu
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Apr 30) 274 (18) 12933-8.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199908
EW 19990801
AB Transforming growth factor (TGF)-beta1 induces extracellular matrix
deposition and proliferation of ***mesenchymal*** cells. We recently
reported that interleukin (IL)-6 is an essential mediator of growth
factor-induced proliferation of lung fibroblasts. Here, we demonstrate by
reverse transcriptase polymerase chain reaction and enzyme-linked
immunoassay that TGF-beta1 is a potent inducer of IL-6 mRNA and protein in
primary human lung fibroblasts. Transient transfections of fibroblasts
with a luciferase reporter ***gene*** ***construct*** containing
nucleotides -651 to +1 of the human IL-6 ***promoter*** revealed that
TGF-beta1 also potently activated IL-6 ***promoter*** activity.
Progressive 5'-deletions and site-directed mutagenesis of the parental
construct located the TGF-beta1-responsive cis-regulatory element to a
known activating protein-1 (AP-1) sequence (nucleotides -284 to -276). Gel
shift analyses revealed that AP-1 DNA binding activity in nuclear extracts
was increased 30 min after stimulation with TGF-beta1. In contrast,
neither CCAAT enhancer-binding protein-beta, NF-kappaB, nor Sp1 were
activated by TGF-beta1. Supershift analyses demonstrated that the AP-1
complex induced by TGF-beta1 was composed of Jun isoforms and absent of
Fos isoforms. Moreover, this complex was found to be a JunD homodimer. Our
data thus demonstrate that TGF-beta1 is a potent inducer of IL-6 in
primary human lung fibroblasts. The TGF-beta1-activated JunD homodimer may
be essential for a majority of the biological effects induced by TGF-beta1
in this cell type, such as proliferation and extracellular matrix
synthesis.

L6 ANSWER 3 OF 12 MEDLINE
AN 1999182460 MEDLINE
DN 99182460
TI COUP-TF upregulates NGFI-A gene expression through an Sp1 binding site.
AU Pipaon C; Tsai S Y; Tsai M J
CS Department of Cell Biology, Baylor College of Medicine, Houston, Texas
77030, USA.
SO MOLECULAR AND CELLULAR BIOLOGY, (1999 Apr) 19 (4) 2734-45.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
EW 19990604
AB The formation of various tissues requires close communication between two
groups of cells, epithelial and ***mesenchymal*** cells. COUP-TFs are

transcription factors which have been shown to have functions in embryonic
development. COUP-TFI is expressed mainly in the nervous system, and its
targeted deletion leads to defects in the central and peripheral nervous
systems. COUP-TFII is highly expressed in the ***mesenchymal*** component of the developing organs. A null mutation of COUP-TFII results
in the malformation of the heart and blood vessels. From their expression
pattern, we proposed that COUP-TFs regulate paracrine signals important
for ***mesenchymal*** cell-epithelial cell interactions. In order to
identify genes regulated by COUP-TF in this process, a rat urogenital
mesenchymal cell line was stably transfected with a COUP-TFI
expression ***vector*** . We found that NGFI-A, a gene with important
functions in brain, organ, and vasculature development, has elevated mRNA
and protein levels upon overexpression of COUP-TFI in these cells. A study
of the ***promoter*** region of this gene identified a
COUP-TF-responsive element between positions -64 and -46. Surprisingly,
this region includes binding sites for members of the Sp1 family of
transcription factors but no COUP-TF binding site. Mutations that abolish
the Sp1 binding activity also impair the transactivation of the NGFI-A
promoter by COUP-TF. Two regions of the COUP-TF molecule are shown
to be important for NGFI-A activation: the DNA binding domain and the
extreme C terminus of the putative ligand binding domain. The C-terminal
region is likely to be important for interaction with coactivators. In
fact, the coactivators p300 and steroid receptor activator 1 can enhance
the transactivation of the NGFI-A ***promoter*** induced by COUP-TFI.
Finally, we demonstrated that COUP-TF can directly interact with Sp1.
Taken together, these results suggest that NGFI-A is a target gene for
COUP-TFs and that the Sp1 family of transcription factors mediates its
regulation by COUP-TFs.

L6 ANSWER 4 OF 12 MEDLINE
AN 1998389728 MEDLINE
DN 98389728
TI Transcriptional activation capacity of the novel PLAG family of zinc
finger proteins.
AU Kas K; Voz M L; Hensen K; Meyen E; Van de Ven W J
CS Laboratory for Molecular Oncology, Center for Human Genetics, University
of Leuven and Flanders Interuniversity Institute for Biotechnology,
Herestraat 49, B-3000 Leuven, Belgium.. koen.kas@med.kuleuven.ac.be
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23026-32.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U81992; GENBANK-AF006005
EM 199812
EW 19981203
AB We have isolated and characterized two novel cDNAs encoding C2H2 zinc
finger proteins showing high sequence homology to PLAG1, a protein
ectopically activated by ***promoter*** swapping or ***promoter***
substitution in pleomorphic adenomas with chromosomal abnormalities at
chromosome 8q12. PLAG1 and the two new PLAG1 family members (PLAGL1 and
PLAGL2) constitute a novel subfamily of zinc finger proteins that
recognize DNA and/or RNA. To examine the potential of the three human
proteins to modulate transcription, we constructed several PLAG/GAL4 DNA
binding domain fusion proteins and measured their ability to activate
transcription of a reporter ***gene*** ***construct*** in
different mammalian cell lines and in yeast. Although the
carboxyl-terminal part of PLAGL1 shows strong overall transcriptional
activity in ***mesenchymal*** (COS-1) and epithelial cells (293), both
PLAG1 and PLAGL2 transactivate in ***mesenchymal*** cells only if
depleted from a repressing region. This effect is less profound in
epithelial cells. These data suggest that the activation in pleomorphic
adenomas of PLAG1 most likely results in uncontrolled activation of
downstream target genes.

L6 ANSWER 5 OF 12 MEDLINE
AN 97444368 MEDLINE
DN 97444368
TI Tissue-specific expression of the L1 cell adhesion molecule is modulated
by the neural restrictive silencer element.
AU Kallunki P; Edelman G M; Jones F S
CS Department of Neurobiology, The Scripps Research Institute and The Skaggs
Institute for Chemical Biology, La Jolla, California 92037, USA.
NC HD33576 (NICHD)
NS34493 (NINDS)
SO JOURNAL OF CELL BIOLOGY, (1997 Sep 22) 138 (6) 1343-54.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
OS GENBANK-U91929
EM 199712
AB The cell adhesion molecule L1 mediates neurite outgrowth and fasciculation
during embryogenesis and mutations in its gene have been linked to a
number of human congenital syndromes. To identify DNA sequences that
restrict expression of L1 to the nervous system, we isolated a previously
unidentified segment of the mouse L1 gene containing the ***promoter***
, the first exon, and the first intron and examined its activity in vitro
and in vivo. We found that a neural restrictive silencer element (NRSE)
within the second intron prevented expression of L1 gene constructs in
nonneural cells. For optimal silencing of L1 gene expression by the
NRSE-binding factor RE-1-silencing transcription factor (REST)/NRSF, both
the NRSE and sequences in the first intron were required. In transgenic
mice, an L1lacZ ***gene*** ***construct*** with the NRSE generated
a neurally restricted expression pattern consistent with the known pattern
of L1 expression in postmitotic neurons and peripheral glia. In contrast,
a similar construct lacking the NRSE produced precocious expression in the
peripheral nervous system and ectopic expression in ***mesenchymal***
derivatives of the neural crest and in mesodermal and ectodermal cells.
These experiments show that the NRSE and REST/NRSF are important
components in restricting L1 expression to the embryonic nervous system.

L6 ANSWER 6 OF 12 MEDLINE
AN 97059146 MEDLINE
DN 97059146
TI Zebrafish Pax9 encodes two proteins with distinct C-terminal
transactivating domains of different potency negatively regulated by
adjacent N-terminal sequences.

AU Nornes S; Mikkola I; Krauss S; Delghandi M; Perander M; Johansen T
CS Departments of Biochemistry, Institute of Medical Biology, University of
Tromso, 9037 Tromso, Norway.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Oct 25) 271 (43) 26914-23.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U40931; GENBANK-U40932
EM 199702
EW 19970204
AB We describe the isolation of cDNA clones for zebrafish Pax9. Pax9
expression was initiated at the end of the segmentation period in ***mesenchymal*** sclerotome cells on both sides of the notochord
similarly to the corresponding mouse and chick genes. Two transcripts,
Pax9a and -b, are generated by alternative splicing. The gene contains 4
exons with exon 3 being included in the Pax9a transcript and spliced out
in the Pax9b transcript. The Pax9a and -b proteins are identical for 212
amino acids from the N terminus but contain distinct C-terminal regions of
131 and 58 amino acids, respectively. The paired domain of Pax9 displayed
a binding-site specificity distinct from Pax6 but similar to Pax1 and -2.
Both Pax9a and -b activated a ***promoter*** containing a paired
domain binding site. However, this activation was observed when low
amounts of Pax9 expression ***vectors*** were used. Higher amounts led
to a sharp decrease in the activation and even turned into repression.
Both the distinct C-terminal regions of Pax9a and -b harbored
transcriptional activating domains of different potency not revealed in
the context of the full-length proteins due to a negative influence of the
N-terminal region including the paired domain.

L6 ANSWER 7 OF 12 MEDLINE
AN 96428457 MEDLINE
DN 96428457
TI The beta 4 integrin subunit is expressed in mouse fibroblasts and
modulated by transforming growth factor-beta 1.
AU Scardigli R; Soddu S; Falcioni R; Crescenzi M; Cimino L; Sacchi A
CS Molecular Oncogenesis Laboratory, Regina Elena Cancer Institute, C.R.S,
Rome, Italy.
SO EXPERIMENTAL CELL RESEARCH, (1996 Sep 15) 227 (2) 223-9.
Journal code: EPB. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199701
EW 19970104
AB Integrin beta 4 subunit is present in association with alpha 6 chain on
both normal and transformed epithelial cells. Recently alpha 6 beta 4
heterodimer was found on the endothelium of medium-sized blood vessels and
on immature thymocytes. In this report we show, by Northern blotting,
indirect immunofluorescence, immunoprecipitation, and Western blotting,
that beta 4 subunit is expressed also on cells of ***mesenchymal***
origin such as fibroblasts, myoblasts, and myotubes. Increased expression
of alpha 6 beta 4 has been related to the aggressive metastatic phenotype
of human and murine carcinomas. The transforming growth factor beta 1
(TGF-beta 1) has been found to modulate the expression of several
integrins and intracellular matrix proteins, as well as to stimulate cell
invasion and metastatic potential. To evaluate whether alpha 6 beta 4
expression is modulated by TGF-beta 1, we transfected 3T3 fibroblasts with
an expression ***vector*** carrying the human TGF-beta 1 cDNA driven
by the SV40 early ***promoter*** . We observed by indirect
immunofluorescence a modification in the subcellular distribution of beta
4 subunit, which acquires a perinuclear localization. This finding
suggests this integrin subunit correlates with the cytoskeletal
reorganization induced by TGF-beta 1.

L6 ANSWER 8 OF 12 MEDLINE
AN 96330323 MEDLINE
DN 96330323
TI The paired-box transcription factor, PAX2, positively modulates expression
of the Wilms' tumor suppressor gene (WT1).
AU Dehbi M; Ghahremani M; Lechner M; Dressler G; Pelletier J
CS Department of Biochemistry, McGill University, Montreal, Quebec, Canada.
SO ONCOGENE, (1996 Aug 1) 13 (3) 447-53.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199611
AB The Wilms' tumor suppressor gene, wt1, encodes a zinc finger protein which
functions as a transcriptional regulator. Expression of the wt1 gene is
developmentally regulated and restricted to a small set of tissues which
include the fetal urogenital system, mesothelium, and spleen. In the
developing kidney, induction of neprohogenesis by the ureter is
accompanied by an increase in expression levels of the Pax-2 gene, a
developmentally and spatially regulated paired-box member. This is
followed by an increase in wt1 expression as ***mesenchymal*** cells
condense and differentiate. In this report, we demonstrate that PAX2
isoforms are capable of transactivating the wt1 ***promoter*** .
Deletion mutagenesis of the wt1 ***promoter*** identified an element
responsible for mediating PAX2 responsiveness, located between nucleotides
-33 and -71 relative to the first wt1 transcription start site. Consistent
with its identity as a PAX responsive element, multimerization of this
mofit upstream of a heterologous minimal ***promoter*** enhanced
reporter activity when co-transfected with a Pax-2 expression
vector . Finally, we demonstrate that PAX2 can stimulate expression
of the endogenous wt1 gene. These results suggest that a role for PAX2
during ***mesenchyme*** -to-epithelium transition in renal development
is to induce wt1 expression.

L6 ANSWER 9 OF 12 MEDLINE
AN 94109538 MEDLINE
DN 94109538
TI Regulation of interleukin-1 and tumor necrosis factor-alpha induced
granulocyte-macrophage colony-stimulating factor gene expression:
potential involvement of arachidonic acid metabolism.
AU Rizzo M T; Boswell H S
CS Division of Hematology/Oncology, Indiana University School of Medicine,
Walter Oncology Center, Indianapolis.
SO EXPERIMENTAL HEMATOLOGY, (1994 Jan) 22 (1) 87-94.
Journal code: EPR. ISSN: 0301-472X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals

EM 199404
AB Signal transduction pathways evoked by interleukin-1 (IL-1) and tumor
necrosis factor-alpha (TNF-alpha) to stimulate expression of other cytokines in ***mesenchymal*** cells are not clearly understood.
Stimulation of the murine bone marrow stromal cell line +/(+)-1.LDA 11
with IL-1 (500 U/ml) in combination with TNF-alpha (500 U/ml) (IL-1 plus
TNF-alpha) induced expression of c-jun mRNA as well as granulocyte-macrophage colony stimulating factor (GM-CSF) mRNA. We
investigated the possibility that arachidonic acid metabolites, acting through protein kinase C (PKC) and perhaps also through the PKC-responsive
transcription factor c-jun/AP-1, may be responsible for regulating GM-CSF
transcription in these stromal cells. Expression of GM-CSF mRNA was
preceded by IL-1 plus TNF-alpha induced arachidonate release (assayed
using the 3H-derivative). Pretreatment of cells with the phospholipase A2
inhibitor quinacrine (20 microM) inhibited accumulation of both c-jun and
GM-CSF mRNA but had no influence on expression of other genes induced by
IL-1 and TNF-alpha, including leukemia inhibitory factor (LIF). In addition, quinacrine partially blocked IL-1 plus TNF-alpha induced 3H-arachidonic acid release from prelabeled stromal cells. Furthermore,
exogenous arachidonate (10 to 50 microM) induced expression of c-jun. To
investigate the role of arachidonate in GM-CSF transcription, we used a
reporter ***vector*** consisting of the murine GM-CSF ***promoter***
linked to firefly luciferase. Transfection efficiency was monitored by
assessing expression of a constitutively active gene, RSV-beta galactosidase. In this system, quinacrine significantly inhibited IL-1 plus TNF-alpha induced GM-CSF transcription assayed with the reporter
construct. Exogenous arachidonic acid alone (10 microM) increased activity
of GM-CSF reporter ***vector*** 1.5-fold over control. These results
are consistent with the hypothesis that arachidonate metabolites are involved in the signaling pathway that leads to IL-1 plus TNF-alpha induced GM-CSF gene expression. Thus, transcriptional activation of GM-CSF
gene is mediated, in part, by the arachidonate cascade.

L6 ANSWER 10 OF 12 MEDLINE
AN 93275635 MEDLINE
DN 93275635
TI Resistance of human fibroblasts to c-fos mediated transformation.
AU Alt M; Grassmann R
CS Institut fur Klinische und Moleular Virologie, Universitat Erlangen-Nurnberg, Germany.
SO ONCOGENE, (1993 Jun) 8 (6) 1421-7.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199309
AB Overexpression of the proto-oncogene c-fos induces transformation of
primary avian and established rodent ***mesenchymal*** cells and tumor
development in transgenic mice. As overexpression of Fos was also found in
several human tumors of ***mesenchymal*** origin, we were interested
whether c-fos is a transforming protein for human cells. Since fos genes
transduced by infection competent ***vectors*** were most efficient in
cellular transformation, expression cassettes of the human c-fos were
introduced into a replication competent herpesvirus saimiri ***vector***
. Infection of human neonatal fibroblasts, cells of ***mesenchymal***
origin, resulted in episomal persistence of the recombinant viral genome
and expression of c-fos in high excess. However careful examination for
transformed phenotype failed to detect any changes in morphology, serum
dependence, anchorage dependence, and life span, suggesting resistance of
human ***mesenchymal*** cells against c-fos mediated transformation.

L6 ANSWER 11 OF 12 MEDLINE
AN 92049310 MEDLINE
DN 92049310
TI The encephalomyocarditis virus internal ribosome entry site allows
efficient coexpression of two genes from a recombinant provirus in cultured cells and in embryos.
AU Ghattas I R; Sanes J R; Majors J E
CS Department of Biochemistry and Molecular Biophysics, Washington University
School of Medicine, St. Louis, Missouri 63110.
SO MOLECULAR AND CELLULAR BIOLOGY, (1991 Dec) 11 (12) 5848-59.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199202
AB Rous sarcoma virus-based retroviral ***vectors*** were constructed to
compare three different approaches for coexpressing two genes in individual infected cells. All ***vectors*** expressed the upstream
gene (lacZ) from the Rous sarcoma virus long terminal repeat, while the
downstream gene (the chloramphenicol acetyltransferase gene [cat] or
v-src) was expressed in one of three ways: from a subgenomic mRNA
generated by regulated splicing, from a strong internal ***promoter***
, or from the encephalomyocarditis virus internal ribosome entry site
(IRES). Both biochemical and immunohistochemical assays of cultured cells
showed that the encephalomyocarditis virus IRES provided the most
efficient means for coexpressing two genes from a single provirus. Most
importantly, most cells infected by a LacZ-IRES-CAT virus expressed both
LacZ and CAT, whereas most cells infected by internal ***promoter***
or regulated splicing ***vectors*** expressed either LacZ or CAT but
not both. In addition, viral titers were highest with IRES ***vectors***
. Presumably, use of the IRES avoids transcriptional controls and RNA
processing steps that differentially affect expression of multiple genes
from internal ***promoter*** and regulated splicing ***vectors*** .
Finally, we injected a LacZ-IRES-v-Src virus into chicken embryos and then
identified the progeny of infected cells with a histochemical stain for
LacZ. LacZ-positive cells in both skin and ***mesenchyme*** displayed
morphological abnormalities attributable to expression of v-src. Thus,
IRES ***vectors*** can be used to coexpress a reporter gene and a
bioactive gene in vivo.

L6 ANSWER 12 OF 12 MEDLINE
AN 89291870 MEDLINE
DN 89291870
TI Characterization of the ***promoter*** region of the human thrombospondin gene. DNA sequences within the first intron increase
transcription.
AU Laherty C D; Gierman T M; Dixit V M

CS Department of Pathology, University of Michigan Medical School, Ann Arbor,
48109.
NC HL39037 (NHLBI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1989 Jul 5) 264 (19) 11222-7.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-J04835
EM 198910
AB Thrombospondin (TSP) is an extracellular matrix glycoprotein whose
synthesis and secretion by ***mesenchymal*** cells is regulated at the
level of gene transcription by platelet-derived growth factor. To examine
the transcriptional regulation of the TSP gene at the molecular level, a
genomic clone containing the human TSP ***promoter*** and flanking
sequence was isolated and characterized. A 3.8-kilobase pair (kb) DNA
fragment containing the first three exons, the first two introns, and 2.2
kb of 5'-flanking region was sequenced, and the site of transcription
initiation was determined by both primer extension and S1 nuclease
mapping. Consensus sequences for several potential regulatory elements
were found in the 5'-flanking sequence, including a TATA box consensus
sequence, TTTAAAA, located 24 base pairs upstream from the transcription
start site. A chimeric gene was constructed containing the first intron,
the first exon, and 2.0 kb of 5'-flanking sequence of the TSP gene fused
to the promoterless gene for chloramphenicol acetyltransferase. When
transfected into COS-1 or NIH3T3 cells this ***gene***
construct was transcribed, indicating the presence of a functional
promoter in the TSP sequence. Transient transfection studies using
deletion mutants of this TSP-chloramphenicol acetyltransferase construct
were performed to locate cis-acting regulatory sequences. The deletion of
flanking sequence 5' to position -234 had little or no effect on
transcriptional activity, whereas deletion of 5'-flanking sequence
extending further in the 3' direction resulted in the gradual loss of
transcriptional activity. The removal of the first intron resulted in a
4-fold decrease in transcript levels, indicating the presence of a
cis-acting positive element(s) in the first intron of the human TSP gene.
This element(s) was further localized to the region between position +576
and position +727.

=> s stromal fibroblast#/ab,bi
'AB' IS NOT A VALID FIELD CODE
0 STROMAL FIBROBLAST#/AB
16247 STROMAL/BI
92189 FIBROBLAST#/BI
443 STROMAL FIBROBLAST#/BI
((STROMAL(W)FIBROBLAST#)/BI)
L7 443 STROMAL FIBROBLAST#/AB,BI

=> s l7(p)(vector# or construct#)/ab,bi
'AB' IS NOT A VALID FIELD CODE
0 VECTOR#/AB
60999 VECTOR#/BI
0 CONSTRUCT#/AB
27034 CONSTRUCT#/BI
L8 11 L7(P)(VECTOR# OR CONSTRUCT#)/AB,BI

=> d 1- bib ab
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 11 MEDLINE
AN 1999086465 MEDLINE
DN 99086465
TI Efficient gene transfer into normal human skeletal cells using recombinant
adenovirus and conjugated adenovirus-DNA complexes.
AU Sommer B; Kuznetsov S A; Robey P G; O'Connell B; Cristiano R J; Young M F
CS Craniofacial and Skeletal Diseases Branch, Building 30, Room 228, National
Institute of Dental Research, National Institutes of Health, Bethesda, MD
20892, USA.
SO CALCIFIED TISSUE INTERNATIONAL, (1999 Jan) 64 (1) 45-9.
Journal code: CGH. ISSN: 0171-967X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
EW 19990503
AB In order to assess efficient DNA gene transfer into human primary cell
cultures derived from the skeleton we tested two viral-based procedures.
First, replication-deficient recombinant adenoviruses (ADV) were used to
infect post-confluent human marrow ***stromal*** ***fibroblasts***
(HMSF) and human trabecular bone (HTB) cells. Both cell types were readily
infected by modified adenoviral ***vectors*** carrying a reporter gene
making this virus an attractive candidate to facilitate DNA gene transfer.
In a second approach we coincubated DNA with ADV that had polylysine (PLL)
covalently attached. With this ADV/PLL/DNA complex, very efficient gene
transfer into multilayered HMSF and HTB cell cultures was observed, and
DNA coincubated with unmodified ADV failed to be effectively transferred.
These data imply that the covalently bound PLL more effectively binds
exogenous DNA, resulting in a highly efficient internalization event in
both cell types. Thus, this latter method has many advantages over
conventional ADV gene transfer procedures. It is simple, rapid, and it
does not require engineering of DNA into the viral genome, thereby
allowing transfer of large fragments of DNA.

L8 ANSWER 2 OF 11 MEDLINE
AN 1998109431 MEDLINE
DN 98109431
TI Endothelial cell-specific expression of tumor necrosis factor-alpha from
the KDR or E-selectin promoters following retroviral delivery.
AU Jaggar R T; Chan H Y; Harris A L; Bicknell R
CS Imperial Cancer Research Fund Molecular Oncology Unit, Institute of
Molecular Medicine, John Radcliffe Hospital, Headington, Oxford, UK.
SO HUMAN GENE THERAPY, (1997 Dec 10) 8 (18) 2239-47.
Journal code: A12. ISSN: 1043-0342.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
EW 19980404
AB The tumor vasculature offers a target for anti-cancer gene therapy which
has the advantages both of good accessibility to systemically delivered
therapy and comparative homogeneity across solid tumor types. We aimed to
develop retroviruses carrying endothelial-specific promoters for the
delivery of genes to proliferating endothelial cells in vitro and to tumor
endothelial cells in vivo. This paper reports the generation of such
retroviral ***vectors*** and the level of expression of murine tumor
necrosis factor-alpha (mTNF-alpha) cDNA following infection into
endothelial cells and ***stromal*** ***fibroblasts***. Retroviral

vectors carrying mTNF-alpha have been generated whose expression
is controlled either by the retroviral long terminal repeat or by 5' proximal promoter sequences from the endothelial-specific kinase insert
domain receptor (KDR)/VEGF receptor and E-Selectin promoters within the
context of a self-inactivating (SIN) ***vector*** backbone. Both KDR
and E-Selectin have been shown to be upregulated on tumor endothelium. A
putative polyadenylation sequence AAATAAA within the E-Selectin promoter
was mutated to permit faithful transmission of retroviral ***vectors***
carrying this promoter. We demonstrate a 10- to 11-fold increase in
mTNF-alpha expression from promoter elements within sEND endothelioma
cells as compared to NIH-3T3 fibroblasts. Suggestions for further
improvements in ***vector*** design are discussed.

L8 ANSWER 3 OF 11 MEDLINE
AN 97322109 MEDLINE
DN 97322109
TI Differential regulation of interstitial collagenase (MMP-1) gene expression by ETS transcription factors.
AU Westermarck J; Seth A; Kahari V M
CS Department of Dermatology, Turku University Central Hospital, Finland.
SO ONCOGENE, (1997 Jun 5) 14 (22) 2651-60.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199709
EW 19970902
AB Expression of interstitial collagenase (MMP-1) has been detected in
stromal ***fibroblasts*** of various malignant tumors. Here,
we have studied the effect of three structurally different ETS
transcription factors (ETS-1, ERGB/Fli-1, and PU.1) on MMP-1 promoter
activity in NIH3T3 fibroblasts. ETS-1 increased the activity of 3.8 kb
MMP-1 promoter ***construct*** up to tenfold, while ERGB/Fli-1 or PU.1
alone had no marked effect on basal promoter activity. ETS-1 also markedly
potentiated enhancement of MMP-1 promoter by both c-Jun and JunB, whereas
ERGB/Fli-1 augmented only the effect of c-Jun. Interestingly, PU.1
abolished induction of MMP-1 promoter by both c-Jun and JunB. Stimulation
of MMP-1 promoter by 12-O-tetradecanoyl phorbol-13-acetate and okadaic
acid was differentially augmented by ETS-1 and ERGB/Fli-1, and abrogated
by PU.1. Co-transfection studies with MMP-1 promoter 5'-deletion
constructs revealed that AP-1 site was necessary for PU.1-elicited
suppression. As compared to control cell lines, PU.1-positive stable cells
exhibited clearly weaker binding of c-Jun and JunD containing AP-1
complexes to MMP-1 promoter AP-1 element, as well as marked reduction in
basal level and induction of c-jun mRNA by 12-O-tetradecanoyl
phorbol-13-acetate and okadaic acid, suggesting a novel mechanism for
PU.1-mediated inhibition of AP-1 dependent gene expression. These results
show that three structurally distinct ETS transcription factors
differently modulate AP-1 dependent upregulation of MMP-1 gene expression.

L8 ANSWER 4 OF 11 MEDLINE
AN 97278888 MEDLINE
DN 97278888
TI Bone formation in vivo: comparison of osteogenesis by transplanted mouse
and human marrow stromal fibroblasts.
AU Krebsbach P H; Kuznetsov S A; Satomura K; Emmons R V; Rowe D W; Robey P G
CS Laboratory of Developmental Biology and Bone Research Branch, National
Institute of Dental Research, National Institutes of Health, Bethesda,
Maryland 20892, USA.
SO TRANSPLANTATION, (1997 Apr 27) 63 (8) 1059-69.
Journal code: WEJ. ISSN: 0041-1337.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199707
EW 19970703
AB BACKGROUND: Marrow ***stromal*** ***fibroblasts*** (MSFs) are
known to contain bone precursor cells. However, the osteogenic potential
of human MSFs has been poorly characterized. The aim of this study was to
compare the osteogenic capacity of mouse and human MSFs after implantation
in vivo. METHODS: After in vitro expansion, MSFs were loaded into a number
of different vehicles and transplanted subcutaneously into immunodeficient
mice. RESULTS: Mouse MSFs transplanted within gelatin, polyvinyl sponges,
and collagen matrices all formed a capsule of cortical-like bone
surrounding a cavity with active hematopoiesis. In transplants of MSFs
from transgenic mice harboring type I procollagen-chloramphenicol
acetyltransferase ***constructs*** , chloramphenicol acetyltransferase
activity was maintained for up to 14 weeks, indicating prolonged bone
formation by transplanted MSFs. New bone formation by human MSFs was more
dependent on both the in vitro expansion conditions and transplantation
vehicles. Within gelatin, woven bone was observed sporadically and only
after culture in the presence of dexamethasone and L-ascorbic acid
phosphate magnesium salt n-hydrate. Consistent bone formation by human
MSFs was achieved only within vehicles containing
hydroxyapatite/tricalcium phosphate ceramics (HA/TCP) in the form of
blocks, powder, and HA/TCP powder-type I bovine fibrillar collagen strips,
and bone was maintained for at least 19 weeks. Cells of the new bone were
positive for human osteonectin showing their donor origin. HA/TCP powder,
the HA/TCP powder-type I bovine fibrillar collagen strips, and HA/TCP
powder held together with fibrin were easier to load and supported more
extensive osteogenesis than HA/TCP blocks and thus may be more applicable
for therapeutic use. CONCLUSIONS: In this article, we describe the
differences in the requirements for mouse and human MSFs to form bone, and
report the development of a methodology for the consistent in vivo
generation of extensive bone from human MSFs.

L8 ANSWER 5 OF 11 MEDLINE
AN 96316852 MEDLINE
DN 96316852
TI Synthesis and secretion of transforming growth factor beta isoforms by
primary cultures of human breast tumour fibroblasts in vitro and their
modulation by tamoxifen.
AU Benson J R; Wakefield L M; Baum M; Colletta A A
CS Hartwell Laboratory, Section of Academic Surgery, Royal Marsden Hospital,
London, UK.
SO BRITISH JOURNAL OF CANCER, (1996 Aug) 74 (3) 352-8.
Journal code: AV4. ISSN: 0007-0920.
CY SCOTLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199611
AB Tamoxifen may mediate its effect in early breast cancer in part

via an
oestrogen receptor (ER)-independent pathway by directly stimulating
fibroblasts to produce the negative paracrine growth factor transforming
growth factor (TGF)-beta. We have previously shown that secretion of this
factor is induced 3-to 30-fold in human fetal fibroblasts in vitro, and by
stromal ***fibroblasts*** in vivo following tamoxifen
treatment of ER-positive and ER-negative breast cancer patients. Primary
cultures of breast tumour fibroblasts have been exposed to tamoxifen for
48 h, and rates of secretion of TGF-beta 1 and TGF-beta 2 measured using a
quantitative immunoassay. Fibroblast strains derived from malignant and
benign tumours produced and secreted similar amounts of TGF-beta 1, but
benign breast tumour fibroblasts secreted significantly higher levels of
TGF-beta 2 compared with fibroblasts of malignant origin. Tamoxifen did
not induce any consistent increase in TGF-beta secretion into the
conditioned medium, but immunofluorescence analysis for the intracellular
form of TGF-beta 1 revealed evidence of increased immunoreactive protein
in tamoxifen-treated fibroblasts, which is localised to the nucleus.
Therefore synthesis of TGF-beta 1 appears to be stimulated by tamoxifen,
but increased secretion may be abrogated in vitro. Furthermore, using
immunocytochemistry and transient transfection with an ER-responsive
reporter ***construct*** , no ER was demonstrable in these fibroblasts
supporting the proposed ER-independent paracrine pathway.

L8 ANSWER 6 OF 11 MEDLINE
AN 95399753 MEDLINE
DN 95399753
TI Heparin inhibits the expression of interleukin-11 and granulocyte-
macrophage colony-stimulating factor in primate bone marrow stromal
fibroblasts through mRNA destabilization.
AU Yang L; Yang Y C
CS Department of Biochemistry, Walther Oncology Center, Indiana University
School of Medicine, Indianapolis 46202, USA..
NC R01DK43105 (NIDDK)
R01HL48819 (NHLBI)
SO BLOOD, (1995 Oct 1) 86 (7) 2526-33.
Journal code: A8G. ISSN: 0006-4971.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199512
AB Interactions between different cytokines, extracellular matrix components,
and various cell types inside the bone marrow microenvironment are
believed to play important roles in the regulation of hematopoiesis. We
observed that both interleukin-1 (IL-1) and 12-O-tetradecanoylphorbol-13-
acetate (TPA) can stimulate the expression of IL-11 and
granulocyte-macrophage colony-stimulating factor (GM-CSF) genes in a
primate bone marrow ***stromal*** ***fibroblast*** cell line,
PU-34. We also found that IL-1 or TPA-stimulated IL-11 and GM-CSF
expression in PU-34 cells can be abolished by heparin, a class of
molecules related to extracellular matrix components, glycosaminoglycans.
Because the growth inhibitory signals provided by extracellular factors
were less understood, the mechanisms of heparin inhibition of IL-11 and
GM-CSF gene expression were further investigated. Our data demonstrate for
the first time that heparin did not alter the transcription of endogenous
IL-11 and GM-CSF genes or an exogenous IL-11 promoter ***construct***
containing an AP-1 sequence. Instead, heparin facilitated the degradation
of the corresponding mRNAs. Through RNA gel shift assays, heparin-mediated
mRNA destabilization was tentatively linked to its competition for mRNA
binding proteins both in the cell-free system and in intact cells.
Collectively, our findings suggest that varying degrees of heparin
inhibition may provide a novel mechanism for the regulation of cytokine
expression during the growth and differentiation of different lineages of
hematopoietic cells.

L8 ANSWER 7 OF 11 MEDLINE
AN 95263438 MEDLINE
DN 95263438
TI Cloning and characterization of the promoter region of the human
keratinocyte growth factor gene.
AU Finch P W; Lengel C; Chedid M
CS Department of Clinical Neuroscience, Brown University, Rhode Island
Hospital, Providence, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 May 12) 270 (19) 11230-7.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U24106
EM 199508
AB Keratinocyte growth factor (KGF), a member of the fibroblast growth factor
family of related proteins, is expressed by ***stromal***
fibroblasts and acts on epithelial cells in a paracrine fashion.
To understand the mechanisms responsible for regulating normal KGF
expression and how these might be altered in disease, the 5'-flanking
region of this gene was cloned. The presence of two KGF transcription
initiation sites was suggested by ribonuclease protection assay and
confirmed by primer extension analysis. Examination of the genomic DNA
sequence revealed the presence of the putative promoter sequences TATTTA
and CCAAT, located 31 and 50 base pairs upstream, respectively, from the
first of the two mRNA start points, and putative initiator sequences
surrounding each transcription start site. Transient transfection into
murine NIH/3T3 fibroblasts demonstrated that the region required for basal
level KGF promoter activity was located between bases -225 and +190.
Inclusion of sequences between -1503 and -775 markedly reduced promoter
activation, indicating the presence of negative regulatory element(s) in
this region. A similar pattern of promoter activation was detected in
human fibroblasts and in murine C2C12 myoblasts. In contrast, no
chloramphenicol acetyltransferase activity was observed in macrophages and
epithelial and lymphoid cells transfected with the same ***constructs***
. Northern blot analysis revealed a strong correlation between KGF RNA
expression and promoter activation in all cells tested. Activation of the
KGF promoter could be induced by the proinflammatory cytokines interleukin
1 and interleukin 6 and by the adenylate cyclase activator forskolin.
Taken together, these results indicate the existence of cis-acting
element(s) responsible for selective activation of the KGF promoter only
in cells that express KGF mRNA and may provide a mechanistic basis for KGF
gene expression during inflammation.

L8 ANSWER 8 OF 11 MEDLINE

AN 95098019 MEDLINE
DN 95098019
TI Spontaneous in vitro immortalization of breast epithelial cells from a
patient with Li-Fraumeni syndrome.
AU Shay J W; Tomlinson G; Piatyszek M A; Gollahon L S
CS Department of Cell Biology and Neurosciences, University of Texas
Southwestern Medical Center at Dallas 75235-9039..
NC CA50195 (NCI)
CA64871 (NCI)
SO MOLECULAR AND CELLULAR BIOLOGY, (1995 Jan) 15 (1) 425-32.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
AB Individuals with germ line mutations in the p53 gene, such as Li-Fraumeni
syndrome (LFS), have an increased occurrence of many types of cancer,
including an unusually high incidence of breast cancer. This report
documents that normal breast epithelial cells obtained from a patient with
LFS (with a mutation at codon 133 of the p53 gene) spontaneously
immortalized in cell culture while the breast ***stromal*** ***fibroblasts*** from this same patient did not. Spontaneous
immortalization of human cells in vitro is an extremely rare event. This
is the first documented case of the spontaneous immortalization of breast
epithelial cells from a patient with LFS in culture. LFS patient breast
stromal ***fibroblasts*** infected with a retroviral ***vector*** containing human papillomavirus type 16 E7 alone were able
to immortalize, whereas stromal cells obtained from patients with
wild-type p53, similarly infected with human papillomavirus type 16 E7,
did not. The present results indicate a protective role of normal pRb-like
functions in breast ***stromal*** ***fibroblasts*** but not in
breast epithelial cells and reinforces an important role of wild-type p53
in the regulation of the normal growth and development of breast
epithelial tissue.

L8 ANSWER 9 OF 11 MEDLINE
AN 95010359 MEDLINE
DN 95010359
TI Basement membrane assembly and differentiation of cultured corneal cells:
importance of culture environment and endothelial cell interaction.
AU Zieske J D; Mason V S; Wasson M E; Meunier S F; Nolte C J; Fukai N; Olsen
B R; Parenteau N L
CS Schepens Eye Research Institute, Harvard Medical School, Boston,
Massachusetts 02114..
NC 9014 (NEI)
R01 EY07334 (NEI)
R01 EY05665
SO EXPERIMENTAL CELL RESEARCH, (1994 Oct) 214 (2) 621-33.
Journal code: EPB. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199501
AB A three-dimensional corneal tissue ***construct*** was used to examine
the effect of culture environment and endothelial cell interaction on
epithelial differentiation and basement membrane assembly. Rabbit corneal
epithelial cells were cultured over rabbit ***stromal*** ***fibroblasts*** in a collagen matrix with or without an underlying
layer of immortalized mouse corneal endothelial cells (Muragaki, Shiota,
Inoue, Ooshima, Olsen, and Ninomiya. (1992) Eur. J. Biochem. 207,
895-902). The cultures were grown submerged or at a dry or moist
interface. Basement membrane, anchoring fibril, and hemidesmosome assembly
was monitored using transmission electron microscopy as well as indirect
immunofluorescence microscopy of laminin, type VII collagen, and alpha 6
integrin. Antibodies against keratin 3 (K3) and alpha-enolase marked
differentiated and undifferentiated corneal epithelial cells,
respectively. When all three cell types were cultured at a moist
interface, hemidesmosomes, anchoring fibrils, and a continuous basement
membrane were observed 2 wk after lifting the cultures to an air-liquid
interface (air-lift). The distribution of alpha-enolase and K3 was
identical to patterns seen in the limbal region of the cornea. Air-lifted
tissue ***constructs*** lacking the endothelial cell layer showed only
limited distribution of laminin and type VII collagen at the
epithelial-matrix junction. alpha 6 Integrin was present along the entire
plasma membrane of the basal cells; epithelial differentiation was not
complete as alpha-enolase was seen in basal and two to three layers of
suprabasal cells. Submerged cultures without endothelial cells did not
express differentiation markers or basement membrane components. These
data indicate that endothelial cell interaction dramatically enhances the
amount and quality of epithelial basement membrane assembly and that
epithelial differentiation is influenced by the type of interface between
tissue, liquid, and air.

L8 ANSWER 10 OF 11 MEDLINE
AN 94260266 MEDLINE
DN 94260266
TI Antibody targeting in metastatic colon cancer: a phase I study of
monoclonal antibody F19 against a cell-surface protein of reactive tumor
stromal fibroblasts.
AU Welt S; Divgi C R; Scott A M; Garin-Chesa P; Finn R D; Graham M; Carswell
E A; Cohen A; Larson S M; Old L J; et al
CS Ludwig Institute for Cancer Research, New York Unit, NY.
NC CA-08748 (NCI)
CA-57486 (NCI)
CA-33049 (NCI)
SO JOURNAL OF CLINICAL ONCOLOGY, (1994 Jun) 12 (6) 1193-203.
Journal code: JCO. ISSN: 0732-183X.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199409
AB PURPOSE: To define the toxicity, imaging, and biodistribution
characteristics of iodine 131-labeled monoclonal antibody F19
(131I-mAbF19). MAbF19 recognizes the fibroblast activation protein (FAP),
a cell-surface glycoprotein not present in most normal tissues, but
abundantly expressed by reactive ***stromal*** ***fibroblasts***
of epithelial cancers, including more than 95% of primary and metastatic
colorectal carcinomas. PATIENTS AND METHODS: 131I-mAbF19 was administered
intravenously to 17 patients with hepatic metastases from colorectal
carcinoma who were scheduled for resection of localized metastases or
insertion of hepatic artery catheter for regional chemotherapy. Seven to 8
days before surgery, patients received 131I-mAbF19 at three dose levels,
with at least four patients entered at each level. RESULTS: No toxicity
associated with intravenous 131I-mAbF19 administration was observed. Tumor

images were obtained on planar and single-photon emission tomography
(SPECT) scans in 15 of 17 patients with hepatic metastases, tumor-infiltrated portal lymph nodes, and/or recurrent pelvic disease. The
smallest lesion visualized was 1 cm in diameter. The optimal time for
tumor imaging was 3 to 5 days after 131I-mAbF19 administration. The use of
image registration techniques allowed precise anatomic localization of
131I-mAbF19 accumulation. Immunohistochemical analysis of biopsy tissues
showed expression of FAP in the tumor stroma (but not in normal liver) in
all patients studied and confirmed that the FAP-positive tumor ***stromal*** ***fibroblasts*** were interposed between the tumor
capillaries and the malignant colon epithelial cells. At the time of
surgery, tumor-to-liver ratios up to 21:1 and tumor-to-serum ratios up to
9:1 were obtained. The fraction of the injected 131I-mAbF19 dose per gram
tumor (%ID/g tumor) localized to hepatic metastases at the time of surgery
ranged from 0.001% to 0.016%. CONCLUSION: The FAP tumor fibroblast antigen
is highly expressed in primary and metastatic colorectal carcinomas and
shows limited expression in normal adult tissues. This highly selective
expression pattern allows imaging of colorectal carcinoma lesions as small
as 1 cm in diameter on 131I-mAbF19 scans. Because of the consistent
presence of FAP in the stroma of epithelial cancers and the accessibility
of FAP-positive tumor ***stromal*** ***fibroblasts*** to
circulating monoclonal antibodies (mAbs), this study suggests possible
diagnostic and therapeutic applications of humanized mAbF19 and mAbF19
constructs with novel immune and nonimmune effector functions.

L8 ANSWER 11 OF 11 MEDLINE
AN 93204185 MEDLINE
DN 93204185
TI Induction of antitumor immunity by interleukin-2 gene-transduced mouse
mammary tumor cells versus transduced mammary stromal fibroblasts.
AU Tsai S C; Gansbacher B; Tait L; Miller F R; Heppner G H
CS Breast Cancer Program, Meyer L. Prentis Comprehensive Cancer Center of
Metropolitan Detroit, Mich. 48201.
SO JOURNAL OF THE NATIONAL CANCER INSTITUTE, (1993 Apr 7) 85 (7) 546-53.
Journal code: J9J. ISSN: 0027-8874.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199306
AB BACKGROUND: Tumor cell-targeted cytokine gene transfer has been used to
generate tumor cell vaccines, but this approach is limited by the need to
establish and implant live tumor cells. PURPOSE: The purpose of this study
was to determine if ***stromal*** ***fibroblasts*** could be used
as an alternative vehicle for delivery of the cytokine interleukin-2
(IL-2) into the tumor microenvironment. We attempted to establish the
feasibility of (a) genetic immunotherapy in a mammary tumor system and (b)
engineering ***stromal*** ***fibroblasts*** as well as tumor
cells. We compared the effects of tumor cell-mediated and ***stromal***
fibroblast -mediated local IL-2 expression on the generation of
antitumor immune responses. METHODS: Retroviral ***vectors***
containing a human IL-2 gene were used to transduce a mouse mammary tumor
line, 4TO7, and an immortalized but nontumorigenic fibroblast line
established from syngeneic mammary fatpads. Expression of the IL-2 gene in
transduced cells was determined by measuring IL-2 secretion, by
RNA-polymerase chain reaction, and by immunochemistry. Groups of 5-12
BALB/c mice were injected with either 4TO7 cells or various doses of
IL-2-secreting 4TO7 cells (4TO7-IL-2); tumor growth was monitored. To test
whether local IL-2 expression by transduced cells could influence the
growth of unmodified tumor cells, we determined tumor development in
groups of mice treated with 4TO7 cells co-injected with either 4TO7-IL-2
cells or IL-2-secreting fibroblasts. RESULTS: 4TO7-IL-2 cells induced
active immunity able to reject the immunizing tumor and to resist
challenge with parental 4TO7 cells on the contralateral side. Mice
pretreated with 4TO7-IL-2 were significantly protected compared with
untreated control animals or mice pretreated with irradiated 4TO7 cells.
The immunity induced by 4TO7-IL-2 cells did not protect against challenge
with another subline, 4T1, which was derived from the same spontaneously
arising mammary tumor as 4TO7. Co-injection of 4TO7 cells with 4TO7-IL-2
cells reduced tumorigenicity, whereas co-injection of 4TO7 cells with IL-2
secreting fibroblasts did not. CONCLUSION: Our results suggest that
induction of anti-tumor immune response by local IL-2 production is most
effective when the helper cytokine is secreted by the tumor cell.
IMPLICATION: Our studies caution against the use of IL-2 gene-transduced
syngeneic stromal cells as an alternative strategy of gene therapy for
cancer. However, they may allow study of the mechanisms of tumor antigen
recognition and the possible involvement of co-stimulatory signals for
effective tumor vaccination by gene-modified cells.

=> s obesity gene or obesity protein or ob gene/ab,bi
'AB' IS NOT A VALID FIELD CODE
48252 OBESITY
418026 GENE
40 OBESITY GENE
(OBESITY(W)GENE)
48252 OBESITY
844860 PROTEIN
1 OBESITY PROTEIN
(OBESITY(W)PROTEIN)
0 OB GENE/AB
15120 OB/BI
418026 GENE/BI
363 OB GENE/BI
((OB(W)GENE)/BI)
L9 398 OBESITY GENE OR OBESITY PROTEIN OR OB GENE/AB,BI

=> s l9(10a)(construct or vector)/ab,bi
'AB' IS NOT A VALID FIELD CODE
0 CONSTRUCT/AB
18002 CONSTRUCT/BI
0 VECTOR/AB
32375 VECTOR/BI
L10 1 L9(10A)(CONSTRUCT OR VECTOR)/AB,BI

=> d

L10 ANSWER 1 OF 1 MEDLINE
AN 96149401 MEDLINE
DN 96149401
TI Transcriptional activation of the mouse obese (ob) gene by CCAAT/enhancer
binding protein alpha.
AU Hwang C S; Mandrup S; MacDougald O A; Geiman D E; Lane M D
CS Department of Biological Chemistry, Johns Hopkins University

School of
Medicine, Baltimore, MD 21205, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
AMERICA, (1996 Jan 23) 93 (2) 873-7.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-S81087
EM 199605

=> d ab

L10 ANSWER 1 OF 1 MEDLINE
AB Like other adipocyte genes that are transcriptionally activated by
CCAAT/enhancer binding protein alpha (C/EBP alpha) during preadipocyte
differentiation, expression of the mouse obese (ob) gene is immediately
preceded by the expression of C/EBP alpha. While the 5' flanking region of
the mouse ob gene contains several consensus C/EBP binding sites, only one
of these sites appears to be functional. DNase I cleavage inhibition
patterns (footprinting) of the ob gene promoter revealed that recombinant
C/EBP alpha, as well as a nuclear factor present in fully differentiated
3T3-L1 adipocytes, but present at a much lower level in preadipocytes,
protects the same region between nucleotides -58 and -42 relative to the
transcriptional start site. Electrophoretic mobility-shift analysis using
nuclear extracts from adipose tissue or 3T3-L1 adipocytes and an
oligonucleotide probe corresponding to a consensus C/EBP binding site at
nucleotides -55 to -47 generated a specific protein-oligonucleotide
complex that was supershifted by antibody against C/EBP alpha. Probes
corresponding to two upstream consensus C/EBP binding sites failed to
generate protein-oligonucleotide complexes. Cotransfection of a C/EBP
alpha expression ***vector*** into 3T3-L1 cells with a series of 5'
truncated ***ob*** ***gene*** promoter constructs activated
reporter gene expression with all constructs containing the proximal C/EBP
binding site (nucleotides -55 to -47). Mutation of this site blocked
transactivation by C/EBP alpha. Taken together, these findings implicate
C/EBP alpha as a transcriptional activator of the ob gene promoter and
identify the functional C/EBP binding site in the promoter.

=> s ob gene and (mesenchymal or marrow stroma# or stromal fibroblast#)/ab,bi
'AB' IS NOT A VALID FIELD CODE
15120 OB
418026 GENE
363 OB GENE
(OB(W)GENE)
0 MESENCHYMAL/AB
10605 MESENCHYMAL/BI
0 MARROW STROMA#/AB
113221 MARROW/BI
26070 STROMA#/BI
1657 MARROW STROMA#/BI
((MARROW(W)STROMA#)/BI)
0 STROMAL FIBROBLAST#/AB
16247 STROMAL/BI
92189 FIBROBLAST#/BI
443 STROMAL FIBROBLAST#/BI
((STROMAL(W)FIBROBLAST#)/BI)
L11 0 OB GENE AND (MESENCHYMAL OR MARROW STROMA# OR STROMAL FIBROBLAST
#)/AB,BI

=> s ltmc#
L12 69 LTMC#

=> s l12 and ob gene/ab,bi
'AB' IS NOT A VALID FIELD CODE
0 OB GENE/AB
15120 OB/BI
418026 GENE/BI
363 OB GENE/BI
((OB(W)GENE)/BI)
L13 0 L12 AND OB GENE/AB,BI

=> s l12 and obesity factor/ab,bi
'AB' IS NOT A VALID FIELD CODE
0 OBESITY FACTOR/AB
48252 OBESITY/BI
417663 FACTOR/BI
9 OBESITY FACTOR/BI
((OBESITY(W)FACTOR)/BI)
L14 0 L12 AND OBESITY FACTOR/AB,BI

=> s obesity factor/ab,bi
'AB' IS NOT A VALID FIELD CODE
0 OBESITY FACTOR/AB
48252 OBESITY/BI
417663 FACTOR/BI
9 OBESITY FACTOR/BI
((OBESITY(W)FACTOR)/BI)
L15 9 OBESITY FACTOR/AB,BI

=> d l- bib ab
YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L15 ANSWER 1 OF 9 MEDLINE
AN 1999125335 MEDLINE
DN 99125335
TI Plasma alkaline phosphatase activity in children and adolescents.
AU Lai S W; Liu C S; Shih H C; Lin C C
CS Department of Family Medicine, China Medical College Hospital, Taichung,
Taiwan.
SO CHUNG-HUA MIN KUO HSIAO ERH KO I HSUEH HUI TSA CHIH, (1998 Nov-Dec) 39 (6)
386-8.
Journal code: 1M6. ISSN: 0001-6578.
CY TAIWAN: Taiwan, Province of China
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 199904
EW 19990403
AB From February to June in 1996, there were 47,800 students for health
examination in Taichung City, Taiwan. The population consisted of the
first and fourth graders of primary schools and the first grader of junior
high schools. We selected 3,452 healthy students for further study by two
stage sampling. In this report, 52.5% of the students were boys, and 47.5%
of the students were girls. The mean age of students was 9.9 +/- 2.4
years. Girls at age 7 and age 10 had higher activity of alkaline
phosphatase than boys at the same age. The peak of alkaline phosphatase
activity in girls occurred at age 10. Alkaline phosphatase activity was
significantly related to weight-length index by multiple regression
analysis ($p < 0.05$). Although clinical application as an ***obesity***
factor still needs further investigation, in the future it may be
well to routinely check this enzyme when assessing childhood obesity.

L15 ANSWER 2 OF 9 MEDLINE
AN 1998386814 MEDLINE
DN 98386814
TI Evaluation of risks for postoperative pulmonary complications using a
preoperative consultation system.
AU Toriyabe M; Yamakage M; Kawamata T; Homma Y; Kurosawa S; Susa Y; Namiki A
CS Department of Anesthesiology, Sapporo Medical University School of
Medicine.
SO MASUI. JAPANESE JOURNAL OF ANESTHESIOLOGY,

(1998 Jul) 47 (7) 888-93.
Journal code: KHR. ISSN: 0021-4892.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
EM 199812
EW 19981201
AB We retrospectively investigated the perioperative management and
postoperative pulmonary complications of patients who had preoperative
respiratory problems and consultations with anesthesiologists. These
patients numbered eight hundred, 23.7% of all patients who had
preoperative consultations, and 40.9% and 62.0% of the 800 had
preoperative and postoperative respiratory management, respectively. Forty
eight patients (6.0%) received postoperative artificial respiration. One
hundred and twenty four patients (15.5%) had some respiratory
complications post-operatively, and 5 patients (0.7%) died mainly because
of the complications. In an evaluation of these patients with the modified
predicted risk factors of Okutsu including the ***obesity*** ***factor*** and smoking history, there was no respiratory complication
in patients under 14 points. Patients with high points of more than 20
included almost all of the patients (114 patients, 91.9%) who had
postoperative respiratory complications. We conclude that our preoperative
consultation system works well and that the modified predicted-risk
factors for postoperative pulmonary complications is useful for the
standardization and objectivity of preoperative patient evaluation.

L15 ANSWER 3 OF 9 MEDLINE
AN 1998295690 MEDLINE
DN 98295690
TI Hyperleptinemia as a component of a metabolic syndrome of cardiovascular
risk.
AU Leyva F; Godsland I F; Ghatei M; Proudler A J; Aldis S; Walton C; Bloom S;
Stevenson J C
CS Wynn Department of Metabolic Medicine, Imperial College School of Medicine
at the National Heart and Lung Institute, London, UK..
f.leyvaleon@ic.ac.uk
SO ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (1998 Jun) 18 (6)
928-33.
Journal code: B89. ISSN: 1079-5642.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
EW 19980902
AB In humans, production of the adipocyte-derived peptide leptin has been
linked to adiposity, insulin, and insulin sensitivity. We therefore
considered that alterations in plasma leptin concentrations could
constitute an additional component of a metabolic syndrome of
cardiovascular risk. To explore this hypothesis, we employed factor
analysis, a multivariate statistical technique that allows reduction of
large numbers of highly intercorrelated variables to composite,
biologically meaningful factors. Seventy-four men [age, 48.4+/-1.3 years
(mean+/-SEM); body mass index (BMI), 25.6+/-0.3 kg/m2] who were free of
coronary heart disease and diabetes underwent anthropometric measurements
(subscapular-to-triceps [S:T] and subscapular-to-biceps [S:B] skinfold
thickness ratios, measurement of fasting plasma leptin, and an intravenous
glucose tolerance test (IVGTT) for assessment of insulin sensitivity.
Plasma leptin concentrations were correlated with BMI (r=0.57, P<0.001),
S:T (r=0.34, P=0.003), S:B (r=0.37, P<0.001), systolic and diastolic blood
pressures (both r=0.24, P=0.044), fasting triglycerides (r=0.31, P=0.007),
serum uric acid (r=0.35, P=0.003), fasting glucose (r=0.32, P=0.003) and
insulin (r=0.33, P=0.004), and IVGTT insulin (r=0.63, P<0.001). A negative
correlation was observed between leptin and insulin sensitivity (r=-0.32,
P=0.006). No significant correlations emerged between plasma leptin
concentrations and age, high density lipoprotein cholesterol, or IVGTT
glucose. In multivariate regression analyses, BMI (standardized
coefficient [SC]=0.40, P=0.001), fasting insulin (SC=0.23, P=0.036), and
IVGTT insulin (SC=0.51, P<0.001) emerged as independent predictors of
plasma leptin concentrations (R2=0.56, P<0.001). After adjustment for BMI,
only IVGTT insulin emerged as a significant predictor of plasma leptin
concentrations (SC=0.56, P<0.001, R2=0.45, P<0.001). Factor analysis of
plasma leptin concentrations and the variables that are considered
relevant to the insulin resistance syndrome revealed a clustering of
plasma leptin concentrations with a factor dominated by insulin resistance
and high IVGTT insulin, separate from a high IVGTT glucose/central
obesity ***factor*** and a high triglyceride/low high density
lipoprotein cholesterol factor. Together, these factors accounted for
55.9% of the total variance in the dataset. In conclusion, interindividual
variations in plasma leptin concentrations are strongly related to the
principal components of the insulin resistance syndrome. Further studies
are needed to determine whether the insulin-leptin axis plays a
coordinating role in this syndrome and whether plasma leptin
concentrations could provide an additional measure of cardiovascular risk.

L15 ANSWER 4 OF 9 MEDLINE
AN 1998097582 MEDLINE
DN 98097582
TI Plasma leptin levels are increased in survivors of acute sepsis:
associated loss of diurnal rhythm, in cortisol and leptin secretion.
AU Bornstein S R; Licinio J; Tauchnitz R; Engelmann L; Negrao A B; Gold P;
Chrousos G P
CS Developmental Endocrinology Branch, NICHD, NIMH, Bethesda, MD 20892, USA.
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1998 Jan) 83 (1) 280-3.
Journal code: HRB. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199804
EW 19980402
AB Recent animal and human studies have suggested that leptin secretion is
closely linked to the functions of the hypothalamic-pituitary-adrenal
(HPA) axis and the immune system, both of which are crucial in influencing
the course and outcome of critical illness. Therefore, we measured basal
plasma leptin levels and examined the circadian secretion of leptin, in
parallel with the hormones of the HPA axis and a key cytokine,
interleukin-6, in critically ill patients with acute sepsis. Sixteen
critically ill patients from the University of Leipzig Intensive Care Unit
were recruited for this study. All of these patients fulfilled the
standard diagnostic criteria for sepsis. Plasma leptin levels were
measured in all patients and controls at 09:00. In addition, in a subgroup
of eight critically ill patients and all of the nine controls plasma
leptin, cortisol, ACTH and interleukin-6 concentrations were measured
every 4 hours for 24 hours. Mean plasma leptin levels were three-fold
higher (18.9 +/- 4.5 ng/ml) in critically ill patients than controls (3.8
+/- 1.0 ng/ml, p < 0.05). Similarly, ACTH levels were lower (7.8 +/- 3.4
pmol/l) in patients than in controls (17.1 +/- 1.5 pmol/l, p < .001),

while plasma cortisol levels were increased (947.6 +/- 144 nmol/l) in
patients compared to controls (361.1 +/- 29, p < 0.001). Morning plasma
interleukin-6 levels were markedly elevated in all patients with sepsis
(1238.0 +/- 543.1 pg/ml) versus controls (6.4 +/- 1.7, p < 0.001). The
controls exhibited a nyctohemeral fluctuation in plasma leptin levels with
peak levels at 23:00; in contrast, septic patients, had no nocturnal rise
of leptin. In healthy controls, plasma leptin and cortisol had reciprocal
circadian rhythms with high nocturnal leptin levels and low nocturnal
cortisol concentrations; in critically ill patients, this relation was
abolished. Mean leptin levels were three-fold higher in patients who
survived the septic episode (25.5 +/- 6.2, n = 10) than in non-survivors
(8.0 +/- 3.7, n = 6, p < 0.01). We conclude that in addition to its
function as an anti- ***obesity*** ***factor*** , leptin may play a
role in a severe stress state such as acute sepsis.

L15 ANSWER 5 OF 9 MEDLINE
AN 1998006747 MEDLINE
DN 98006747
TI Ventilatory response to CO2 in patients with snoring, obstructive
hypopnoea and obstructive apnoea.
AU Appelberg J; Sundstrom G
CS Department of Clinical Physiology/Mid-Sweden Research and Development
Centre, Vasternorrland County Council, Sundsvall Hospital, Sweden.
SO CLINICAL PHYSIOLOGY, (1997 Sep) 17 (5) 497-507.
Journal code: DKG. ISSN: 0144-5979.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
EW 19980204
AB Obstructive sleep apnoea (OSA) is caused by an obstruction of the upper
airway. Sufficient sensitivity to CO2 in the respiratory centre is known
to be a critical factor for adequate tone in the upper airway muscles. The
hypothesis of this study is, therefore, that the ventilatory response to
CO2 is reduced in patients with OSA. Twenty-six patients who suffered from
snoring, 19 snoring patients with obstructive hypopnoea (OH) and 33
snoring patients with obstructive apnoea (OA), were studied. The control
group consisted of 25 subjects from a random sample with no history of
snoring or daytime sleepiness. Tests of the hyperoxic and hypoxic
ventilatory response to CO2 were performed, as well as static and dynamic
spirometry. Subjects in the OA group displayed a higher hyperoxic
(VE/FetCO2hy = 12.6 l min-1/%) and hypoxic (VE/FetCO2ho = 15.7 l min-1/%)
ventilatory response to CO2 than patients with obstructive hypopnoea
(VE/FetCO2hy = 8.6 l min-1/%; VE/FetCO2ho = 15.2 l min-1/%), snorers
(VE/FetCO2hy = 8.4 l min-1/%; VE/FetCO2ho = 12.7 l min-1/%) and
non-snorers (VE/FetCO2hy = 7.6 l min-1/%; VE/FetCOho = 9.6 l min-1/%).
Multiple regression analysis reveals that neck circumference, apnoea
index, oxygen desaturation index, PCO2 and sex (male gender) are
correlated with VE/FetCO2hy (R2 = 0.43). Multiple regression analysis also
reveals that ERV (expiratory reserve volume) and sex (male gender) are
correlated with VE/FetCO2ho (R2 = 0.21). Arguing against the hypothesis,
patients with OSA displayed an increased hyperoxic and hypoxic ventilatory
response to CO2. Nocturnal apnoea frequency and the ***obesity***
factor in OSA may have contributed to these results.

L15 ANSWER 6 OF 9 MEDLINE
AN 96067418 MEDLINE
DN 96067418
TI Hemostatic function in young subjects with central obesity: relationship
with left ventricular function.
AU Licata G; Scaglione R; Avellone G; Ganguzza A; Corrao S; Arnone S; Di
Chiara T
CS Department of Internal Medicine, University of Palermo, Italy..
SO METABOLISM: CLINICAL AND EXPERIMENTAL, (1995 Nov) 44 (11) 1417-21.
Journal code: MUM. ISSN: 0026-0495.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199602
AB This study was designed to evaluate coagulation and fibrinolysis activity
and their relationship with left ventricular function in young obese
subjects with central fat distribution. We assessed coagulation and
fibrinolysis activity by evaluation of factor VII activity, fibrinogen and
plasminogen, plasminogen activator inhibitor (PAI), and tissue plasminogen
activator antigen basally (tPA1) and after venous occlusion (tPA2). These
measures were evaluated in young (< 40 years) obese subjects with central
fat distribution (n = 19) and in comparable lean subjects (n = 20). Blood
glucose, triglycerides, total and high-density lipoprotein (HDL)
cholesterol, apolipoprotein (apo) A1 and apo B, fasting immunoreactive
insulin, and lipoprotein(a) levels were also measured by current methods.
Left ventricular ejection fraction (LVEF) and peak filling rate (PFR)
determined by radionuclide angiocardiography and left ventricular mass
(LVM) and LVM indexed for body height (LVM/H) determined by
echocardiographic study were calculated. Central obesity was evaluated by
the waist to hip ratio (WHR) according to the criteria of the Italian
Consensus Conference of ***Obesity*** . ***Factor*** VII (P <
.001), fibrinogen (P < .001), plasminogen (P < .001), PAI activity (P <
.001), tPA1 (P < .02), fasting blood glucose (P < .01), apo B (P < .02),
and immunoreactive insulin (P < .01) were significantly higher in obese
than in lean subjects. In contrast, HDL cholesterol (P < .01), tPA2 (P <
.01), LVEF (P < .001), and PFR (P < .02) were significantly lower in obese
than in lean subjects. In all subjects, WHR correlated directly with
fibrinogen and inversely with tPA2; LVEF correlated inversely with tPA1,
PAI, and fibrinogen; and PFR correlated inversely with factor VII
activity.(ABSTRACT TRUNCATED AT 250 WORDS)

L15 ANSWER 7 OF 9 MEDLINE
AN 92076056 MEDLINE
DN 92076056
TI Correlation between changes in obesity from adolescence to young adulthood
and family obesity--the results of cross sectional and longitudinal
studies.
AU Wada J; Ueda K
CS Fukuoka Prefectural Dazaifu Hospital..
SO NIPPON KOSHU EISEI ZASSHI [JAPANESE JOURNAL OF PUBLIC HEALTH], (1990 Oct)
37 (10) 837-42.
Journal code: A9J. ISSN: 0546-1766.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
EM 199203
AB We conducted a survey of 356 married couples and their 552 children living

in Hisayama in Fukuoka prefecture in order to investigate the correlation between changes in obesity from adolescence to young adulthood. 1. A positive correlation between couples in weight and height could be found, but its coefficient was weak (r = 0.12, 0.10). There was no correlation between couples in BMI. 2. The correlation between parents and their children in height, weight and BMI was significantly positive (r = 0.18, 0.45), having a coefficient greater than that of the correlation between married couples. 3. The correlation coefficient between mother and child was greater than that of the correlation coefficient between father and child. 4. The BMI of a child with either parent obese was significantly greater than that of a child with neither parent obese. Obesity appeared more frequently in children whose BMI of parent was higher. 5. A positive correlation between the BMI of young adults and that of adolescents could be found, and the average BMI of the obesity group was higher than that of the non-obesity group even in the adolescent subjects. 6. Even after considering BMI during adolescence, the familial factor had a significant relationship to the BMI of young adulthood. These results suggest that obesity in adolescence will influence obesity in young adulthood, and that the appearance of obesity strongly correlates with the familial ***obesity*** ***factor*** . In conclusion, it is very important to take preventative measures, in cooperation with the family, early in a child's adolescent years in order to avoid obesity in adulthood.

L15 ANSWER 8 OF 9 MEDLINE
AN 88118430 MEDLINE
DN 88118430
TI Psychological status of morbidly obese women before gastric restriction surgery.
AU Hafner R J; Watts J M; Rogers J
CS Dibden Research Unit, Glenside Hospital, Eastwood, South Australia..
SO JOURNAL OF PSYCHOSOMATIC RESEARCH, (1987) 31 (5) 607-12.
Journal code: JUV. ISSN: 0022-3999.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198805
AB One hundred and eighteen of 142 morbidly obese women had gastric restriction surgery after completing self-report questionnaire measures of psychosocial adjustment as part of their preoperative psychiatric assessment. Compared with an age-matched normal population, they scored significantly higher on measures of phobic anxiety, somatization, depression, hostility, and marital dissatisfaction, the last being associated mainly with later onset ***obesity*** . ***Factor*** analysis of questionnaire and weight data showed that weight was largely independent of psychological adjustment, although associations occurred when analysis was restricted to the data on married women, in which marital and self-assertion abnormalities loaded significantly on the same factor.

L15 ANSWER 9 OF 9 MEDLINE
AN 82215497 MEDLINE
DN 82215497
TI Response to fibrinolytic activity and factor VIII-related antigen to stimulation with desmopressin in hyperlipoproteinemia.
AU Brommer E J; Gevers Leuven J A; Barrett-Bergshoeff M M; Schouten J A
SO JOURNAL OF LABORATORY AND CLINICAL MEDICINE, (1982 Jul) 100 (1) 105-14.
Journal code: IVR. ISSN: 0022-2143.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198210
AB Impairment of fibrinolysis is supposed to contribute to CVD. In 38 hyperlipoproteinemic patients, known to be at risk for early CVD, fibrinolytic activity was measured before and after stimulation with DDAVP. A negative correlation was found between serum triglyceride levels and fibrinolytic activity, both before and after DDAVP. A subnormal activity was invariably found when serum triglyceride concentration was above 8 mmol/L. The defect can be attributed to low levels of extrinsic plasminogen activator. High cholesterol levels were not associated with impairment of fibrinolysis. Fibrinolytic activity and response to DDAVP were lowest in those patients with hypertriglyceridemia who also had a tendency to develop hyperchylomicronemia. (type V/IV). The low fibrinolytic activity in this type of hyperlipoproteinemia cannot be explained by ***obesity*** . ***Factor*** VIII was higher than normal in most patients with hyperlipoproteinemia; the level increased after stimulation with DDAVP in every patient. This imbalance between coagulation and fibrinolysis might increase the risk of CVD.

```
=> s leptin/ab,bi
'AB' IS NOT A VALID FIELD CODE
         0 LEPTIN/AB
      1867 LEPTIN/BI
L16    1867 LEPTIN/AB,BI

=> s l16 and adipocyte#/ab,bi
'AB' IS NOT A VALID FIELD CODE
         0 ADIPOCYTE#/AB
      8138 ADIPOCYTE#/BI
L17     385 L16 AND ADIPOCYTE#/AB,BI

=> s adipocyte#/ab,bi
'AB' IS NOT A VALID FIELD CODE
         0 ADIPOCYTE#/AB
      8138 ADIPOCYTE#/BI
L18    8138 ADIPOCYTE#/AB,BI

=> s l18(10a)(construct or exogenous or vector)/ab,bi
'AB' IS NOT A VALID FIELD CODE
         0 CONSTRUCT/AB
     18002 CONSTRUCT/BI
         0 EXOGENOUS/AB
     52796 EXOGENOUS/BI
         0 VECTOR/AB
     32375 VECTOR/BI
L19      54 L18(10A)(CONSTRUCT OR EXOGENOUS OR VECTOR)/AB,BI

=> s l19 and (ob gene or leptin)/ab,bi
'AB' IS NOT A VALID FIELD CODE
         0 OB GENE/AB
     15120 OB/BI
    418026 GENE/BI
       363 OB GENE/BI
           ((OB(W)GENE)/BI)
         0 LEPTIN/AB
      1867 LEPTIN/BI
L20      1 L19 AND (OB GENE OR LEPTIN)/AB,BI

=> d bib ab

L20 ANSWER 1 OF 1 MEDLINE
AN 96214975 MEDLINE
DN 96214975
TI Regulation of expression of ob mRNA and protein by glucocorticoids and
```

cAMP.
AU Slieker L J; Sloop K W; Surface P L; Kriauciunas A; LaQuier F; Manetta J;
Bue-Valleskey J; Stephens T W
CS Endocrine Research and Technology Core Divisions, Lilly Research
Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46285, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Mar 8) 271 (10) 5301-4.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199608
AB Regulation of obese gene (ob) expression in ob/ob and db/db mice and in
cultured rat ***adipocytes*** was examined. It has been demonstrated
that ***exogenous*** human OB protein (***leptin***) treatment
reduces food intake and weight gain, as well as insulin, glucose, and
corticosterone levels in ob/ob mice. In the present report we show that
leptin treatment down-regulates endogenous adipose ob mRNA.
However, treatment of isolated rat adipocytes with 100 ng/ml human or
murine ***leptin*** had no direct effect on expression of endogenous
ob mRNA, suggesting that ***leptin*** may be able to down-regulate its
own expression by an indirect, non-autocrine mechanism. Glucocorticoids
increased both ob mRNA levels and secreted ***leptin*** levels in
vitro. Conversely, agents that increase intracellular cAMP, such as
beta-adrenergic agonists or Bt2cAMP itself, decreased ob mRNA expression
and ***leptin*** secretion. Therefore, increased glucocorticoid levels
and decreased sympathetic neural activity may contribute to the elevated
ob mRNA expression observed in genetically obese, hyperglucocorticoid
rodents. Furthermore, ***leptin*** might regulate its own expression
through a feedback mechanism involving the hypothalamic pituitary axis.

=> d his

(FILE 'HOME' ENTERED AT 15:12:44 ON 18 OCT 1999)

FILE 'MEDLINE' ENTERED AT 15:12:49 ON 18 OCT 1999

L1 142 S STROMA#(P)(EXOGENOUS GENE OR GENE CONSTRUCT OR VECTOR)/AB,BI
L2 26 S L1 AND PROMOTER#/AB,BI
L3 1 S L2 AND COLLAGEN/AB,BI
L4 14675 S MESENCHYM?/AB,BI
L5 64 S L4(P)(GENE CONSTRUCT OR EXOGENOUS GENE OR VECTOR#)/AB,BI
L6 12 S L5 AND PROMOTER#/AB,BI
L7 443 S STROMAL FIBROBLAST#/AB,BI
L8 11 S L7(P)(VECTOR# OR CONSTRUCT#)/AB,BI
L9 398 S OBESITY GENE OR OBESITY PROTEIN OR OB GENE/AB,BI
L10 1 S L9(10A)(CONSTRUCT OR VECTOR)/AB,BI
L11 0 S OB GENE AND (MESENCHYMAL OR MARROW STROMA# OR STROMAL FIBROBL
L12 69 S LTMC#
L13 0 S L12 AND OB GENE/AB,BI
L14 0 S L12 AND OBESITY FACTOR/AB,BI
L15 9 S OBESITY FACTOR/AB,BI
L16 1867 S LEPTIN/AB,BI
L17 385 S L16 AND ADIPOCYTE#/AB,BI
L18 8138 S ADIPOCYTE#/AB,BI
L19 54 S L18(10A)(CONSTRUCT OR EXOGENOUS OR VECTOR)/AB,BI
L20 1 S L19 AND (OB GENE OR LEPTIN)/AB,BI

=> s l1 or l4
L21 14812 L1 OR L4

=> s l21 and (ob gene or leptin)/ab,bi
'AB' IS NOT A VALID FIELD CODE
0 OB GENE/AB
15120 OB/BI
418026 GENE/BI
363 OB GENE/BI
((OB(W)GENE)/BI)
0 LEPTIN/AB
1867 LEPTIN/BI
L22 0 L21 AND (OB GENE OR LEPTIN)/AB,BI

=> file medline embase biosis inpadoc caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 17.29 17.56

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=> s l22
'AB' IS NOT A VALID FIELD CODE
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'AB' IS NOT A VALID FIELD CODE
L23 2 L22

=> dup rem l23
PROCESSING COMPLETED FOR L23
L24 2 DUP REM L23 (0 DUPLICATES REMOVED)

=> d l- bib ab
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L24 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN 1997:717829 CAPLUS
DN 128:18701
TI Use of ob protein for inducing bone formation
IN Durnam, Diane M.; Kuijper, Joseph L.; Weigle, David S.; Liu, Chung C.
PA Zymogenetics, Inc., USA; University of Washington
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9739767	A1	19971030	WO 1997-US6892	19970418

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG

CA 2251808	AA	19971030	CA 1997-2251808	19970418
AU 9728104	A1	19971112	AU 1997-28104	19970418
EP 917469	A1	19990526	EP 1997-922438	19970418

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

PRAI US 1996-15647 19960419
WO 1997-US6892 19970418
AB Methods for inducing bone formation using ob protein (***leptin***)
are disclosed. The methods can be used for treating osteoporosis, repairing fractures, dental defects, resectioning due to oncogenesis and
elongation of the growth plate/long bone. In addn., the methods can be
used for ex vivo therapy and reinfused into a mammal.

L24 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1999 ACS
AN 1997:802782 CAPLUS
DN 128:73875
TI Hepatic fibrosis, glomerulosclerosis, and a lipodystrophy-like syndrome in
PEPCK-TGF-.beta.1 transgenic mice
AU Clouthier, David E.; Comerford, Sarah A.; Hammer, Robert E.
CS Department of Biochemistry, Howard Hughes Medical Institute, University
Texas Southwestern Medical Center, Dallas, TX, 75235-9050, USA
SO J. Clin. Invest. (1997), 100(11), 2697-2713
CODEN: JCINAO; ISSN: 0021-9738
PB Rockefeller University Press
DT Journal
LA English
AB Transgenic mice overexpressing a constitutively active human TGF-.beta.1
under control of the rat phosphoenolpyruvate carboxykinase regulatory
sequences developed fibrosis of the liver, kidney, and adipose tissue, and
exhibited a severe redn. in body fat. Expression of the transgene in
hepatocytes resulted in increased collagen deposition, altered lobular
organization, increased hepatocyte turnover, and in extreme cases, hemorrhage and thrombosis. Renal expression of the transgene was
localized to the proximal tubule epithelium, and was assocd. with
tubulointerstitial fibrosis, characterized by excessive collagen
deposition and increased fibronectin and plasminogen activator inhibitor-1
immunoreactivity. Pronounced glomerulosclerosis was evident, and
hydronephrosis developed with low penetrance. Expression of TGF-.beta.1
in white and brown adipose tissue resulted in a lipodystrophy-like
syndrome. All white fat depots and brown fat pads were severely reduced
in size, and exhibited prominent fibroplasia. This redn. in white fat was
due to impaired adipose accretion. Introduction of the transgene into the
ob/ob background suppressed the obesity characteristic of this mutation;
however, transgenic mutant mice developed severe hepato- and splenomegaly.
These studies strengthen the link between TGF-.beta.1 expression and
fibrotic disease, and demonstrate the potency of TGF-.beta.1 in modulating
mesenchymal cell differentiation in vivo.

=> d his

(FILE 'HOME' ENTERED AT 15:12:44 ON 18 OCT 1999)

FILE 'MEDLINE' ENTERED AT 15:12:49 ON 18 OCT 1999
L1 142 S STROMA#(P)(EXOGENOUS GENE OR GENE CONSTRUCT OR VECTOR)/AB,BI
L2 26 S L1 AND PROMOTER#/AB,BI
L3 1 S L2 AND COLLAGEN/AB,BI
L4 14675 S MESENCHYM?/AB,BI
L5 64 S L4(P)(GENE CONSTRUCT OR EXOGENOUS GENE OR VECTOR#)/AB,BI
L6 12 S L5 AND PROMOTER#/AB,BI
L7 443 S STROMAL FIBROBLAST#/AB,BI
L8 11 S L7(P)(VECTOR# OR CONSTRUCT#)/AB,BI
L9 398 S OBESITY GENE OR OBESITY PROTEIN OR OB GENE/AB,BI
L10 1 S L9(10A)(CONSTRUCT OR VECTOR)/AB,BI
L11 0 S OB GENE AND (MESENCHYMAL OR MARROW STROMA# OR STROMAL FIBROBL
L12 69 S LTMC#
L13 0 S L12 AND OB GENE/AB,BI
L14 0 S L12 AND OBESITY FACTOR/AB,BI
L15 9 S OBESITY FACTOR/AB,BI
L16 1867 S LEPTIN/AB,BI
L17 385 S L16 AND ADIPOCYTE#/AB,BI
L18 8138 S ADIPOCYTE#/AB,BI
L19 54 S L18(10A)(CONSTRUCT OR EXOGENOUS OR VECTOR)/AB,BI
L20 1 S L19 AND (OB GENE OR LEPTIN)/AB,BI
L21 14812 S L1 OR L4
L22 0 S L21 AND (OB GENE OR LEPTIN)/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 15:28:51 ON 18
OCT 1999
L23 2 S L22
L24 2 DUP REM L23 (0 DUPLICATES REMOVED)

=> s obesity protein or obesity factor or obesity gene or ob gene or leptin/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L25 9655 OBESITY PROTEIN OR OBESITY FACTOR OR OBESITY GENE OR OB GENE OR
LEPTIN/AB,BI

=> s l25 and (stroma# or mesenchymal or adipocyte#)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L26 1681 L25 AND (STROMA# OR MESENCHYMAL OR ADIPOCYTE#)/AB,BI

=> s l25 and (construct# or vector# or exogenous)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L27 363 L25 AND (CONSTRUCT# OR VECTOR# OR EXOGENOUS)/AB,BI

=> s l27 and (stroma# or mesenchymal or adipocyte#)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L28 79 L27 AND (STROMA# OR MESENCHYMAL OR ADIPOCYTE#)/AB,BI

=> dup rem l28
PROCESSING COMPLETED FOR L28
L29 35 DUP REM L28 (44 DUPLICATES REMOVED)

=> d l- bib ab
YOU HAVE REQUESTED DATA FROM 35 ANSWERS - CONTINUE? Y/(N):y

L29 ANSWER 1 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1999:565879 CAPLUS
DN 131:179821
TI Isolated ***stromal*** cells for use in the treatment of diseases of
the central nervous system
IN Prockop, Darwin J.; Stokes, David G.; Azizi, S. Ausim; Phinney, Donald G.
PA MCP Hahnemann University, USA
SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9943286	A2	19990902	WO 1999-US3897	19990224

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,

SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-28395 19980224
AB Methods of treating a human patient having a disease, disorder or condition of the central nervous system are disclosed. The methods include obtaining a bone marrow sample from a human donor, isolating ***stromal*** cells from the bone marrow sample, and administering the isolated ***stromal*** cells to the central nervous system of the human patient, wherein the presence of the isolated ***stromal*** cells in the brain effects treatment of the disease, disorder or condition. Stomal cells which are isolated may be cultured in vitro, they may be genetically engineered to produce therapeutic compds., and/or they may be pre-differentiated prior to administration into the central nervous system.

L29 ANSWER 2 OF 35 MEDLINE
AN 1999162615 MEDLINE
DN 99162615
TI Reversing ***adipocyte*** differentiation: implications for treatment of obesity.
AU Zhou Y T; Wang Z W; Higa M; Newgard C B; Unger R H
CS Gifford Laboratories, Center for Diabetes Research, University of Texas Southwestern Medical Center, Dallas, TX 75235, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Mar 2) 96 (5) 2391-5.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199906
EW 19990603
AB Conventional treatment of obesity reduces fat in mature ***adipocytes*** but leaves them with lipogenic enzymes capable of rapid resynthesis of fat, a likely factor in treatment failure. Adenovirus-induced hyperleptinemia in normal rats results in rapid nonketotic fat loss that persists after hyperleptinemia disappears, whereas pair-fed controls regain their weight in 2 weeks. We report here that the hyperleptinemia depletes ***adipocyte*** fat while profoundly down-regulating lipogenic enzymes and their transcription factor, peroxisome proliferator-activated receptor (PPAR)gamma in epididymal fat; enzymes of fatty acid oxidation and their transcription factor, PPARalpha, normally low in ***adipocytes*** , are up-regulated, as are uncoupling proteins 1 and 2. This transformation of ***adipocytes*** from cells that store triglycerides to fatty acid-oxidizing cells is accompanied by loss of the ***adipocyte*** markers, ***adipocyte*** fatty acid-binding protein 2, tumor necrosis factor alpha, and ***leptin*** , and by the appearance of the preadipocyte marker Pref-1. These findings suggest a strategy for the treatment of obesity by alteration of the ***adipocyte*** phenotype.

L29 ANSWER 3 OF 35 MEDLINE DUPLICATE 1
AN 1999195492 MEDLINE
DN 99195492
TI Transcriptional regulation of fatty acid synthase gene by insulin/glucose, polyunsaturated fatty acid and ***leptin*** in hepatocytes and ***adipocytes*** in normal and genetically obese rats.
AU Fukuda H; Iritani N; Sugimoto T; Ikeda H
CS Tezukayama Gakuin College, Sakai, Osaka, Japan.
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1999 Mar) 260 (2) 505-11.
Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199907
EW 19990701
AB Transcriptional regulation of the fatty acid synthase (FAS) gene by insulin/glucose, polyunsaturated fatty acids and ***leptin*** was investigated in hepatocytes and ***adipocytes*** of Wistar fatty rats and their lean littermates. The sequence spanning nucleotides -57 to -35 of FAS gene, which is responsive to insulin/glucose stimulation [Fukuda, H., Iritani, N. & Noguchi, T. (1997) FEBS Lett. 406, 243-248], was linked to a reporter gene containing a heterologous promoter and transfected into rat hepatocytes or ***adipocytes*** . The activity of the reporter, chloramphenicol acetyltransferase, in the presence of glucose alone was similar in the primary cultured cells from the lean and obese rats. In the presence of insulin/glucose, however, chloramphenicol acetyltransferase activity was markedly increased in hepatocytes of lean rats, but was not significantly increased in those of obese rats. The stimulation by insulin/glucose was reduced in arachidonic acid-treated cells of lean rats. Similarly, the stimulation by insulin/glucose was reduced in ***leptin*** -treated cells and in cells from lean rats containing an expression ***vector*** encoding ***leptin*** . However, neither polyunsaturated fatty acids nor ***leptin*** -treated cells from obese rats responded to insulin-stimulation. The same effects were observed at endogenous FAS mRNA and enzyme levels. Similar results were seen in ***adipocytes*** , although the stimulation and suppression were much smaller than in hepatocytes. The insulin-binding capacities of the receptors of liver and adipose tissue were reduced in the presence of ***leptin*** or polyunsaturated fatty acids. ***Leptin*** and polyunsaturated fatty acids appeared to suppress the insulin stimulation of FAS transcription by reducing the insulin-binding capacities of receptors. ***Leptin*** converged on the insulin/glucose response element of FAS gene and suppressed the transcription.

L29 ANSWER 4 OF 35 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 1999303784 EMBASE
TI Regulation of ATP citrate-lyase gene expression in hepatocytes and ***adipocytes*** in normal and genetically obese rats.
AU Fukuda H.; Iritani N.
CS N. Iritani, Tezukayama Gakuin College, 4-2-2 Harumidai, Sakai, Osaka 590-0113, Japan
SO Journal of Biochemistry, (1999) 126/2 (437-444).
Refs: 41
ISSN: 0021-924X CODEN: JOBIAO
CY Japan
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB Transcriptional regulation of ATP citrate-lyase (ACL, one of the lipogenic enzymes) gene by glucose/insulin, polyunsaturated fatty acid (PUFA), and ***leptin*** has been investigated in hepatocytes and

adipocytes
of obese Wistar fatty rats and their lean littermates. The sequence spanning nucleotides -64 to -41 of the ACL gene, which is responsive to glucose/insulin stimulation, was linked to a reporter gene and transfected into rat hepatocytes or ***adipocytes*** . The chloramphenicol acetyltransferase (CAT) activities in the presence of glucose alone were similar in primary cultured cells from both obese and lean rats. In the presence of glucose/insulin, however, the CAT activities were markedly increased in the hepatocytes of lean rats, but were not significantly increased in those of obese rats. The stimulation by glucose/insulin was reduced in PUFA-treated cells of lean rats. The stimulation was also reduced in ***leptin*** -treated cells or ***ob*** ***gene*** expression ***vector*** -containing cells. However, PUFA- or ***leptin*** -treated cells from obese rats did not show a significant reduction in insulin stimulation. The same effects were observed at the endogenous mRNA and enzyme levels. Similar results were seen in ***adipocytes*** , although the stimulation and suppression levels were much smaller than in hepatocytes. The expression of endogenous insulin receptor in hepatocytes and ***adipocytes*** was reduced in the presence of ***leptin*** or PUFA. We previously found that insulin-binding capacities are also reduced in the presence of ***leptin*** or PUFA and are very low in obese rats in comparison with lean. Moreover, gel mobility shift assays using end-labeled ACL-(-64/-41) revealed that nuclear factor(s) including Sp1 bind specifically to the sequence, and DNA-protein complex formation is reduced in the obese rats. Thus, the reductions in the insulin-stimulated ACL transcription may be ascribed in part to reductions in insulin binding to receptors and DNA-protein complex formation.

L29 ANSWER 5 OF 35 MEDLINE DUPLICATE 2
AN 1999208214 MEDLINE
DN 99208214
TI Growth hormone in obesity.
AU Scacchi M; Pincelli A I; Cavagnini F
CS University of Milan, IRCCS Ospedale San Luca, Istituto Auxologico Italiano, Italy.
SO INTERNATIONAL JOURNAL OF OBESITY AND RELATED METABOLIC DISORDERS, (1999 Mar) 23 (3) 260-71. Ref: 150
Journal code: BTX. ISSN: 0307-0565.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199907
EW 19990704
AB Growth hormone (GH) secretion, either spontaneous or evoked by provocative stimuli, is markedly blunted in obesity. In fact obese patients display, compared to normal weight subjects, a reduced half-life, frequency of secretory episodes and daily production rate of the hormone. Furthermore, in these patients GH secretion is impaired in response to all traditional pharmacological stimuli acting at the hypothalamus (insulin-induced hypoglycaemia, arginine, galanin, L-dopa, clonidine, acute glucocorticoid administration) and to direct somatotrope stimulation by ***exogenous*** growth hormone releasing hormone (GHRH). Compounds thought to inhibit hypothalamic somatostatin (SRIH) release (pyridostigmine, arginine, galanin, atenolol) consistently improve, though do not normalize, the somatotropin response to GHRH in obesity. The synthetic growth hormone releasing peptides (GHRPs) GHRP-6 and hexarelin elicit in obese patients GH responses greater than those evoked by GHRH, but still lower than those observed in lean subjects. The combined administration of GHRH and GHRP-6 represents the most powerful GH releasing stimulus known in obesity, but once again it is less effective in these patients than in lean subjects. As for the peripheral limb of the GH-insulin-like growth factor I (IGF-I) axis, high free IGF-I, low IGF-binding proteins 1 (IGFBP-1) and 2 (IGFBP-2), normal or high IGFBP-3 and increased GH binding protein (GHBP) circulating levels have been described in obesity. Recent evidence suggests that ***leptin*** , the product of ***adipocyte*** specific ***ob*** ***gene*** , exerts a stimulating effect on GH release in rodents; should the same hold true in man, the coexistence of high ***leptin*** and low GH serum levels in human obesity would fit in well with the concept of a ***leptin*** resistance in this condition. Concerning the influence of metabolic and nutritional factors, an impaired somatotropin response to hypoglycaemia and a failure of glucose load to inhibit spontaneous and stimulated GH release are well documented in obese patients; furthermore, drugs able to block lipolysis and thus to lower serum free fatty acids (NEFA) significantly improve somatotropin secretion in obesity. Caloric restriction and weight loss are followed by the restoration of a normal spontaneous and stimulated GH release. On the whole, hypothalamic, pituitary and peripheral factors appear to be involved in the GH hyposecretion of obesity. A SRIH hypertone, a GHRH deficiency or a functional failure of the somatotrope have been proposed as contributing factors. A lack of the putative endogenous ligand for GHRP receptors is another challenging hypothesis. On the peripheral side, the elevated plasma levels of NEFA and free IGF-I may play a major role. Whatever the cause, the defect of GH secretion in obesity appears to be of secondary, probably adaptive, nature since it is completely reversed by the normalization of body weight. In spite of this, treatment with biosynthetic GH has been shown to improve the body composition and the metabolic efficacy of lean body mass in obese patients undergoing therapeutic severe caloric restriction. GH and conceivably GHRPs might therefore have a place in the therapy of obesity.

L29 ANSWER 6 OF 35 MEDLINE DUPLICATE 3
AN 1999115205 MEDLINE
DN 99115205
TI ***Leptin*** 's actions on the reproductive axis: perspectives and mechanisms.
AU Cunningham M J; Clifton D K; Steiner R A
CS Graduate Program in Neurobiology & Behavior, University of Washington, Department of Obstetrics and Gynecology, Seattle, USA.
SO BIOLOGY OF REPRODUCTION, (1999 Feb) 60 (2) 216-22. Ref: 123
Journal code: A3W. ISSN: 0006-3363.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English

FS Priority Journals
EM 199906
EW 19990603
AB Energy availability influences reproductive fitness. The activity of the reproductive axis is sensitive to the adequacy of nutrition and the stores of metabolic reserves. The ***adipocyte*** -derived hormone ***leptin*** is postulated to reflect the state of nutrition and energy reserves and serve as a metabolic gate to the reproductive system. Genetically obese ob/ob mice (lacking endogenous ***leptin***) are infertile, and treatment of these animals with ***exogenous*** ***leptin*** stimulates the activity of the reproductive endocrine system and induces fertility in both sexes. Severely food-restricted animals have reduced circulating levels of ***leptin*** , which are associated with markedly reduced secretion of the gonadotropins, LH, and FSH. Treatment of food-restricted mice, rats, sheep, and monkeys with ***exogenous*** ***leptin*** reverses the diet-induced inhibition of gonadotropin secretion. ***Leptin*** has also been suggested to have a role in timing the onset of puberty in several species, although evidence that ***leptin*** is the primary metabolic signal for initiating the onset of puberty in any species is controversial. Notwithstanding this debate, it is undisputed for all species studied to date that adequate levels of ***leptin*** in the circulation are essential (but not sufficient) for pubertal progression and that ***leptin*** treatment can reverse the delay in sexual maturation caused by food restriction. Double-label in situ hybridization studies in the brain of the mouse, rat, and monkey have revealed that hypothalamic neurons expressing proopiomelanocortin and neuropeptide Y coexpress the ***leptin*** receptor, whereas no evidence has been adduced that GnRH neurons express this receptor. Together, these observations suggest that ***leptin*** is a metabolic signal to the neuroendocrine reproductive system and that under conditions of inadequate energy reserves, low ***leptin*** levels act as a metabolic "gate" to inhibit the activity of the neuroendocrine reproductive axis in both sexes.

L29 ANSWER 7 OF 35 MEDLINE DUPLICATE 4

AN 1999093439 MEDLINE
DN 99093439
TI ***Leptin*** is an endogenous protective protein against the toxicity exerted by tumor necrosis factor.
AU Takahashi N; Waelput W; Guisez Y
CS Molecular Pathophysiology and Experimental Therapy Unit, Department of Molecular Biology, Flanders Interuniversity Institute for Technology, University of Ghent, B-9000 Ghent, Belgium.. nozomi.takahashi@dumb.rug.ac. be
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1999 Jan 4) 189 (1) 207-12. Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199904
EW 19990404
AB Tumor necrosis factor (TNF) is a central mediator of a number of important pathologies such as the systemic inflammatory response syndrome. Administration of high TNF doses induces acute anorexia, metabolic derangement, inflammation, and eventually shock and death. The in vivo effects of TNF are largely mediated by a complex network of TNF-induced cytokines and hormones acting together or antagonistically. Since TNF also induces ***leptin*** , a hormone secreted by ***adipocytes*** that modulates food intake and metabolism, we questioned the role of ***leptin*** in TNF-induced pathology. To address this question, we tested mouse strains that were defective either in ***leptin*** gene (ob/ob) or in functional ***leptin*** receptor gene (db/db), and made use of a receptor antagonist of ***leptin*** . Ob/ob and db/db mice, as well as normal mice treated with antagonist, exhibited increased sensitivity to the lethal effect of TNF. ***Exogenous*** ***leptin*** afforded protection to TNF in ob/ob mice, but failed to enhance the protective effect of endogenous ***leptin*** in normal mice. We conclude that ***leptin*** is involved in the protective mechanisms that allow an organism to cope with the potentially autoaggressive effects of its immune system.

L29 ANSWER 8 OF 35 MEDLINE DUPLICATE 5

AN 1999355448 MEDLINE
DN 99355448
TI Transcriptional regulation of ***leptin*** gene promoter in rat.
AU Fukuda H; Iritani N
CS Faculty of Human and Cultural Studies, Tezukayama Gakuin University, Sakai, Osaka, Japan.
SO FEBS LETTERS, (1999 Jul 16) 455 (1-2) 165-9. Journal code: EUH. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199910
EW 19991003
AB To investigate the DNA regulatory sequences required for stimulation and suppression of ***leptin*** gene expression, primary cultured hepatocytes and ***adipocytes*** of rats were transfected with plasmids containing the 5'-flanking sequences of the rat ***leptin*** gene fused to the luciferase gene. When two copies of the sequences spanning nucleotides -101 to -83 of the ***leptin*** promoter were used for transfection, the reporter activity significantly increased in the presence of glucose/insulin in comparison with glucose alone. The glucose/insulin stimulation of the transcription was inhibited by addition of polyunsaturated fatty acids. These results were similar to those found earlier for the transcription of the fatty acid synthase, FAS(-57/-35) and ATP citrate-lyase, ACL(-64/-41) genes. Cotransfection studies in the cells with a Sp1 expression ***vector*** and ***leptin*** (-101/-83) ***constructs*** showed the inactivation of the ***leptin*** promoter by Sp1. Gel mobility shift assays using an end-labeled ***leptin*** (-101/-83) ***construct*** as a probe revealed that nuclear factor(s) from rat liver or adipose tissue specifically formed complexes with the sequence. The DNA-protein complexes were common to the glucose/insulin-responsive regions of the ***leptin*** , ACL and FAS genes, suggesting that these genes are coordinately regulated. In addition, by antibody supershift assays, the transcription factor Sp1 was found to bind the GC-rich region located between nucleotides -101 and -83 of the ***leptin*** gene. Mutational analysis of this region showed that the sequence of the region was critical for glucose/insulin stimulation of transcription. Thus, we postulated that the region

from
-101 to -83 of the ***leptin*** gene is responsible for glucose/insulin stimulation of transcription, and that Sp1 is somehow involved in this regulation.

L29 ANSWER 9 OF 35 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1999:248934 BIOSIS
DN PREV199900248934
TI Mechanisms of TNF-alpha-induced insulin resistance.
AU Hotamisligil, G. S. (1)
CS (1) Division of Biological Sciences and Department of Nutrition, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA, 02115 USA
SO Experimental and Clinical Endocrinology & Diabetes, (1999) Vol. 107, No. 2, pp. 119-125. ISSN: 0947-7349.
DT Article
LA English
SL English
AB There is now substantial evidence linking TNF-alpha to the presentation of insulin resistance in humans, animals and in vitro systems. We explored the relationship between TNF-alpha and insulin resistance using knockout mice deficient for either TNF-alpha or one or both of its receptors, p55 and p75. In studies of TNF-alpha-deficient knockout mice with diet-induced obesity, obese TNF-alpha knockouts responded to an ***exogenous*** dose of insulin or glucose much more efficiently than TNF-alpha wild-type animals. This finding suggests that deletion of TNF-alpha leads to increased insulin sensitivity, ie decreased insulin resistance. In studies using genetically obese ob/ob mice, TNF-alpha receptor wild-type and p75 receptor knockout animals developed a pronounced hyperinsulinemia and transient hyperglycaemia, whereas p55 receptor and double-knockout animals did not. Moreover, in glucose and insulin tolerance tests, we found that p75 knockout animals exhibited profiles identical to those of the wild-type animals, but that p55 knockout animals and double mutants showed a mild improvement in insulin sensitivity, relative to the wild type. Since the improvement in sensitivity was slightly greater with double mutants, p55 alone cannot be responsible for TNF-alpha's promotion of insulin resistance in obese mice, despite the likelihood that it is more important than p75. How TNF-alpha-related insulin resistance is mediated is not fully clear, although phosphorylation of serine residues on IRS-1 has previously been shown to be important. When we monitored Glut 4 expression in obese TNF-alpha wild-type and knockout mice, we found no convincing evidence that TNF-alpha mediation of the downregulation of Glut 4 mRNA expression is responsible for insulin resistance. However, we found an approximately 2-fold increase in insulin-stimulated tyrosine phosphorylation of the insulin receptor in the muscle and adipose tissue of TNF-alpha knockout mice, suggesting that insulin receptor signalling is an important target for TNF-alpha. Other possible mediators of TNF-alpha-induced insulin resistance include circulating free fatty acids (FFAs) and ***leptin*** .

L29 ANSWER 10 OF 35 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 1999074781 EMBASE
TI Serum ***leptin*** as an additional possible pathogenic factor in polycystic ovary syndrome.
AU El Orabi H.; Ghalia A.A.; Khalifa A.; Mahfouz H.; El Shalkani A.; Shoieb N.
CS Dr. A.A. Ghalia, Oncology Diagnostic Unit, Ain Shams Faculty of Medicine, Abbassia, Cairo, Egypt
SO Clinical Biochemistry, (1999) 32/1 (71-75). Refs: 27 ISSN: 0009-9120 CODEN: CLBIAS
PUI S 0009-9120(98)00091-5
CY United States
DT Journal; Article
FS 010 Obstetrics and Gynecology
029 Clinical Biochemistry
LA English
SL English
AB Objectives: Recent data raised the possibility that high ***leptin*** levels may contribute to infertility in some women with PCOS. Design and methods; To assess changes in ***leptin*** levels and its relationship to some hormonal changes (insulin, testosterone, SHBG, FSH, LH, and prolactin) associated with PCOS in obese (n = 27) and nonobese (n = 18) patients when compared to obese and nonobese normal controls (n = 20). Results: ***Leptin*** concentration were significantly higher in PCOS than in controls, $p < 0.05$, with 81% sensitivity and 50% specificity. Whereas, high serum insulin levels were found in obese and nonobese women with PCOS, high serum ***leptin*** , FAI together with reduced SHBG were found in obese rather than nonobese PCOS women. Moreover, hyperleptinemia in PCOS women was not correlated to hyperinsulinemia (r = - 0.13 and -0.4 in obese and nonobese PCOS women, respectively). In the patient's group correlation analysis between fasting serum ***leptin*** and different studied variables showed some correlation with body mass index (BMI) only (r = 0.413) suggesting that high ***leptin*** levels could be a characteristic of the obese PCOS. However, multiregression analysis showed that together with testosterone, ***leptin*** can successfully predict the presence or absence of PCOS. Conclusion: The potential significance of ***leptin*** for the pathophysiology of PCOS will await direct studies of the effects of ***exogenous*** ***leptin*** and/or its inhibitors on the reproductive axis of women, including those with PCOS.

L29 ANSWER 11 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1999:349750 CAPLUS
DN 131:144032
TI Study on mechanism of high-fat and sucrose diets in obesity development in rats
AU Xue, Changyong; Zheng, Zixin; Zhang, Rongxin; Zhang, Xiaoliang; Li, Xiya; Inoue, Shuji
CS Department of Nutrition, General Hospital of Chinese PLA, Beijing, 100853, Peop. Rep. China
SO Yingyang Xuebao (1999), 21(1), 42-47 CODEN: YYHPA4; ISSN: 0512-7955
PB Yingyang Xuebao Bianjibu
DT Journal
LA Chinese
AB To gain insight into mechanisms whereby high-fat and sucrose diets affect triglyceride metab. and induce obesity, changes in fasting plasma triglyceride levels, hepatic triglyceride secretion and clearance rate, insulin and lipoprotein lipase were obsd. in ventromedial hypothalamus (VMH)-lesioned normal rats. A high-fat diet had a potency to increase body wt. and body fat, but a high-sucrose diet only had an effect in

increasing body fat. Both diets could cause increase in plasma insulin concn. Increased insulin level promoted enhancement in activity of lipoprotein lipase. A high-fat diet led to increase in ***exogenous*** triglyceride in blood, which was rapidly transferred into ***adipocyte*** under action of lipoprotein lipase. A high sucrose diet caused increase in insulin concn. which was a stimulation factor for hepatic prodn. of endogenous triglycerides. The endogenous triglycerides entered ***adipocyte*** under action of increased lipoprotein lipase. Mechanisms by which high-fat and sucrose diets lead to obesity are different. The difference is that a high-fat diet induces increase in ***exogenous*** triglycerides, and a high-sucrose diet induces overprodn. of endogenous triglycerides. However, both diets have the same aspect, i.e. both diets cause hyperinsulinemia. Increased insulin level leads to enhancement of lipoprotein activity which promotes entrance of increased triglyceride into ***adipocyte*** .

L29 ANSWER 12 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1998:112467 CAPLUS
DN 128:176972
TI Human ***leptin*** receptor gene-related protein and its nucleic acids and therapeutic applications
IN Akerblom, Ingrid E.
PA Incyte Pharmaceuticals, Inc., USA; Akerblom, Ingrid E.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9805792	A2	19980212	WO 1997-US14191	19970725
US 5789198	A	19980804	US 1996-691071	19960801
US 5874535	A	19990223	US 1997-843370	19970415
EP 920503	A2	19990609	EP 1997-937213	19970725

W: AT, BR, CA, CH, CN, DE, ES, FI, GB, IL, JP, KR, MX, NO, NZ, RU, SE, SG, US, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
R: BE, DE, ES, FR, GB, IT, NL
PRAI US 1996-691071 19960801
US 1997-843370 19970415
WO 1997-US14191 19970725

AB The present invention provides a polynucleotide which identifies and encodes a novel human ***leptin*** receptor gene-related protein (LRGRP). LRGRP shares part of its nucleic acid-coding sequences with a noncoding region of human ***leptin*** receptor cDNA and has homol. to the membrane-assocd. proteins of Caenorhabditis elegans ORF C30B5.2 and Saccharomyces cerevisiae ORF YJR044c. Portions of cDNAs unique to LRGRP were found in heart, placenta, lung, liver, skeletal muscle, kidney, pancreas, brain, pre- ***adipocyte*** cell lines both before and after differentiation, as well as in 6 hematopoietic cells lines and a cervical cancer cell line. The LRGRP gene maps to the same site and the ***leptin*** receptor on human chromosome 1p31. The genomic organization of the gene encoding LRGRP and the sequence of the exon/intron junction are provided. The invention also provides expression ***vectors*** , host cells, agonists, and antagonists. The invention also provides methods for treating metabolic, reproductive, connective tissue and neoplastic disorders.

L29 ANSWER 13 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1998:106005 CAPLUS
DN 128:176963
TI Porcine ***leptin*** protein, nucleic acid sequences coding therefor and uses thereof
IN Bidwell, Christopher A.; Spurlock, Michael E.
PA Purina Mills, Inc., USA; Purdue Research Foundation; Bidwell, Christopher A.; Spurlock, Michael E.
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9804690	A1	19980205	WO 1997-US12483	19970717

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9738028 A1 19980220 AU 1997-38028 19970717
PRAI US 1996-692922 19960731
WO 1997-US12483 19970717

AB A porcine ***adipocyte*** -specific polypeptide, termed ***leptin*** , is expressed in the fat tissue of pigs. Expression may be altered in over fat pigs, or expression may be in the form of a protein of lesser biol. activity relative to that of leaner pigs. The porcine ***adipocyte*** polypeptide, DNA and RNA mols. coding therefor, methods for its prepn., and antibodies specific for the polypeptide are disclosed. The nucleotide sequence of the porcine ***leptin*** gene comprising 5917 bp, cDNA comprising 501 bp, and the amino acid translation of the ***leptin*** coding sequences (166 amino acids including signal peptide) are provided. The gene contains 2 exons. There was 83% identity between the pig and human cDNA sequence and a 76% identity between pig and mouse cDNA sequence. Methods for detg. the susceptibility of a pig to fat deposition are based on measuring the levels of the porcine ***adipocyte*** polypeptide in a biol. fluid or tissue ext. or by measuring mRNA encoding the porcine ***adipocyte*** polypeptide in cells of the subject. Methods of evaluating an agent related to the deposition of fat in swine comprise contacting the agent with an ***adipocyte*** in vitro and measuring the amt. of the porcine ***adipocyte*** polypeptide or mRNA that is produced by the ***adipocyte*** . Methods of limiting fat deposition include administering porcine ***leptin*** or porcine ***leptin*** DNA, and methods of regulating intake include administering porcine ***leptin*** , porcine ***leptin*** DNA, or an antibody directed against porcine ***leptin*** .

L29 ANSWER 14 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1998:98346 CAPLUS
DN 128:184666
TI Bovine ***leptin*** protein, nucleic acid sequences coding therefor, and uses thereof
IN Spurlock, Michael E.
PA Purina Mills, Inc., USA; Spurlock, Michael E.
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
---------- ---- -------- ---------- --------
PI WO 9804288 A1 19980205 WO 1997-US12532 19970717
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG
AU 9736032 A1 19980220 AU 1997-36032 19970717
PRAI US 1996-688908 19960731
WO 1997-US12532 19970717
AB A bovine ***adipocyte*** -specific polypeptide, termed ***leptin***
, is expressed in the fat tissue of cattle. Expression may be altered in
overly fat cattle, or expression may be in the form of a protein of lesser
biol. activity relative to that of leaner cattle. The bovine
adipocyte polypeptide, DNA and RNA mols. coding therefor, methods
for its prepn., and antibodies specific for the polypeptide are disclosed.
Methods for detg. the susceptibility of cattle to fat deposition are based
on measuring the levels of the bovine ***adipocyte*** polypeptide in a
biol. fluid or tissue ext. or by measuring mRNA encoding the bovine
adipocyte polypeptide in cells of the subject. Methods of
evaluating an agent related to the deposition of fat in cattle comprise
contacting the agent with an ***adipocyte*** in vitro and measuring
the amt. of the bovine ***adipocyte*** polypeptide or mRNA that is
produced by the ***adipocyte*** . Methods of limiting fat deposition
include administering ***leptin*** or ***leptin*** DNA, and
methods of altering intake include administering ***leptin*** ,
leptin DNA, or an antibody directed against ***leptin*** .

L29 ANSWER 15 OF 35 MEDLINE DUPLICATE 6
AN 1998326258 MEDLINE
DN 98326258
TI Serum ***leptin*** levels in male marathon athletes before and after
the marathon run.
AU Leal-Cerro A; Garcia-Luna P P; Astorga R; Parejo J; Peino R; Dieguez C;
Casanueva F F
CS Division of Endocrinology, Hospital Virgen del Rocio, Sevilla, Spain.
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1998 Jul) 83 (7)
2376-9.
Journal code: HRB. ISSN: 0021-972X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199810
EW 19981001
AB ***Leptin*** is a hormone produced by the ***adipocytes*** to
regulate food intake and energy expenditure at the hypothalamic level. It
is commonly accepted that the main determinants of ***leptin***
secretion are the net amount of body fat and the mean size of
adipocytes . On the contrary, important ***vectors*** of energy
flux in the organism, such as food intake and energy expended on exercise,
are not thought to be regulators of that secretion. To understand whether
leptin is regulated by an acute energy expenditure such as
strenuous exercise, 29 male athletes who had trained for marathon running
were studied before and after a marathon run and compared with 22
nonobese, age-, sex-, and body mass index (BMI)-matched sedentary
controls. Controls and marathon athletes showed no differences in BMI or
fat-free mass. Marathon runners showed a strong reduction in total fat
mass (6.2 +/- 0.4 kg; 9.1 +/- 0.5% of body fat) compared with controls
(12.3 +/- 0.5 kg; 16.1 +/- 0.5% of body fat; P < 0.05). This difference in
body composition was paralleled by a mean serum ***leptin*** level
that in marathonians (2.9 +/- 0.2 micrograms/L) was significantly (P <
0.05) reduced compared with that in controls (5.1 +/- 0.6 micrograms/L).
It is remarkable that the ratio of ***leptin*** per kg body fat,
showed a very good agreement between the two groups, 0.40 +/- 0.04
microgram/L.kg for controls and 0.46 +/- 0.03 microgram/L.kg for
marathonians. In the two groups, ***leptin*** was correlated with both
body weight, BMI, and fat mass (P < 0.001). The marathon trajectory was
the standard 42.195 km accomplished in an average time of 3 h, 17 min, 7
s, with a calculated energy expenditure of over 2800 Cal. After the
marathon run, a water imbalance occurred, with a significant decrease in
body weight and an increase in serum albumin. A significant (P < 0.05)
reduction in ***leptin*** values was observed after the run (2.6 +/-
0.2 micrograms/L) compared with before (2.9 +/- 0.2 micrograms/L), which
was more relevant considering the relative hemoconcentration. In
conclusion, 1) compared with sedentary subjects, ***leptin*** levels
are reduced in male marathon runners in parallel with the relevant
reduction in total body fat; 2) expressed as a ratio of ***leptin***
per kg body fat, no differences were observed between marathonians and
controls; and 3) after an energy expenditure of 2800 Cal in the marathon
run, a reduction in ***leptin*** levels occurred. Strong changes in
energy expenditure may regulate serum ***leptin*** levels in man.

L29 ANSWER 16 OF 35 MEDLINE DUPLICATE 7
AN 1998283266 MEDLINE
DN 98283266
TI The biology of ***leptin*** : a review.
AU Houseknecht K L; Baile C A; Matteri R L; Spurlock M E
CS Department of Animal Sciences, Purdue University, West Lafayette, IN
47907, USA.
SO JOURNAL OF ANIMAL SCIENCE, (1998 May) 76 (5) 1405-20. Ref: 176
Journal code: HC7. ISSN: 0021-8812.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199809
EW 19980902
AB ***Leptin*** , a 16-kDa protein secreted from white ***adipocytes***
, has been implicated in the regulation of food intake, energy expenditure, and whole-body energy balance in rodents and humans. The gene
encoding ***leptin*** was identified by positional cloning and

is the
mutation leading to the profound obese phenotype of the ob/ob mouse.
Exogenous administration of ***leptin*** to ob/ob mice leads
to a significant improvement in reproductive and endocrine status as well
as reduced food intake and weight loss. The expression and secretion of
leptin is highly correlated with body fat mass and
adipocyte size. Cortisol and insulin are potent stimulators of
leptin expression, and expression is attenuated by beta-adrenergic
agonists, cAMP, and thiazolidinediones. The role of other hormones and
growth factors in the regulation of ***leptin*** expression and
secretion is emerging. ***Leptin*** circulates specifically bound to
proteins in serum, which may regulate its half-life and biological
activity. Isoforms of the ***leptin*** receptor, members of the
interleukin-6 cytokine family of receptors, are found in multiple tissues,
including the brain. Many of ***leptin*** 's effects on food intake and
energy expenditure are thought to be mediated centrally via
neurotransmitters such as neuropeptide Y. Multiple peripheral effects of
leptin have also been recently described, including the regulation
of insulin secretion by pancreatic beta cells and regulation of insulin
action and energy metabolism in ***adipocytes*** and skeletal muscle.
Leptin is thought to be a metabolic signal that regulates
nutritional status effects on reproductive function. ***Leptin*** also
plays a major role in hematopoeisis and in the anorexia accompanying an
acute cytokine challenge. The profound effects of ***leptin*** on
regulating body energy balance make it a prime candidate for drug
therapies for humans and animals.

L29 ANSWER 17 OF 35 MEDLINE DUPLICATE 8
AN 1999093082 MEDLINE
DN 99093082
TI Fasting serum ***leptin*** levels in the analysis of body mass index
cut-off values: are they useful for overweight screening in children and
adolescents? A school population-based survey in three provinces of
central Italy.
AU Falorni A; Galmacci G; Bini V; Papi F; Molinari D; De Giorgi G; Faraoni F;
Celi F; Di Stefano G; Berioli M G; Contessa G; Bacosi M L
CS Clinica Pediatrica, Servizio Regionale di Diabetologia Pediatrica, Universit' a di Perugia, Italy.
SO INTERNATIONAL JOURNAL OF OBESITY AND RELATED METABOLIC DISORDERS, (1998 Dec) 22 (12) 1197-208.
Journal code: BTX. ISSN: 0307-0565.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
EW 19990305
AB OBJECTIVE: Body mass index (BMI) was determined in a population of school
students from three provinces of central Italy. Fasting serum ***leptin*** concentrations were assayed in a large number of subjects
from the same area, to determine their distribution as plotted against the
standard deviation score (z-score) of BMI. DESIGN, SUBJECTS AND
MEASUREMENTS: Height and weight were recorded from 31170 subjects (16175
male and 14995 female), aged 3-18 y, to ***construct*** BMI charts of
children and adolescents from central Italy. Percentiles and z-score were
calculated using the LMS method of Cole. Serum ***leptin*** concentrations were assayed in 1929 subjects (996 male and 933 female)
after overnight fasting. RESULTS: BMI percentiles of central Italy were
higher than those from standards of other European and USA populations.
When plotted against the z-score of BMI, serum ***leptin*** values
were distributed according to an exponential curve, showing a steep
pattern and a wide distribution, as BMI values increased. The hypothesis
of the existence of two subgroups, based on a different relation between
leptin and BMI, was verified and a separation point between the
two subgroups was identified using cluster analysis, discriminant analysis
and a novel method developed by our group, hereafter referred to as
'regression clustering'. This method allows identification of the value of
the independent variable (z-score of BMI) which can be taken as a
separation point. This analysis provided the best results and indicated
the following separation points: central Italy standard, z-score = 0.72
(76.4th percentile) for males and z-score = 0.69 (75.5th percentile) for
females; French standard (the one suggested for a European population by
the European Childhood Obesity Group, ECOG), z-score = 1.46 (92.8th
percentile) for males and z-score = 1.96 (97.5th percentile) for females.
Similar but variable results were obtained when the same analysis was
performed on serum ***leptin*** concentration, subdivided according to
pubertal development (stage I, stage II-III, stage IV-V).
CONCLUSIONS:
Children and adolescents from central Italy had greater BMI percentiles
when compared to other European populations. Fasting serum ***leptin***
concentrations showed a distribution pattern related to z-score, thus
allowing to identification of two different subgroups. The z-scores of
BMI, identified as separation points, indicated a trend to ***leptin***
production by ***adipocytes*** that could be taken as indicators of
significant increases of fat mass. This study proposes criteria and a
statistical approach that could be useful in the identification of BMI
cut-off values when screening children and adolescents for overweight.

L29 ANSWER 18 OF 35 MEDLINE DUPLICATE 9
AN 1998289621 MEDLINE
DN 98289621
TI ***Leptin*** gene transfer into muscle increases lipolysis and oxygen
consumption in white fat tissue in ob/ob mice.
AU Marti A; Novo F J; Martinez-Anso E; Zaratiegui M; Aguado M; Martinez J A
CS Department of Physiology and Nutrition, University of Navarra, Pamplona,
Spain.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1998 May 29) 246 (3)
859-62.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199809
EW 19980902
AB The effects of ***leptin*** production in ob/ob mice injected with a
plasmid expression ***vector*** containing mouse ***leptin*** cDNA
in the tibialis anterior muscle were investigated. A significant reduction
in food intake (-18%, $p < 0.01$) along the experimental period was found

after DNA injection, while differences in body weight gain were only
significant (-41%, $p < 0.05$) when determined between days 2.9 of the
study. Concerning ***adipocytes*** metabolism, there was a significant
increase in oxygen consumption in vitro (+34%, $p < 0.05$) and in basal
lipolysis (+151%, $p < 0.05$) in DNA-injected mice compared to PBS-injected
animals. Our results confirm that functional ***leptin*** can be
produced in muscle and released into the blood stream and give new support
to the fact that ***leptin*** may have direct auto- or paracrine
effects on ***adipocytes*** , possible contributing to the weight- and
fat-reducing effects of ***leptin*** in ob/ob mice.

L29 ANSWER 19 OF 35 MEDLINE
AN 1999072323 MEDLINE
DN 99072323
TI Functional analysis of the C(-188)A polymorphism of the human
leptin promoter.
AU Oksanen L; Palvimo J J; Janne O A; Kontula K
CS Department of Medicine, Institute of Biomedicine, University of Helsinki,
Finland.
SO HUMAN GENETICS, (1998 Oct) 103 (4) 527-8.
Journal code: GED. ISSN: 0340-6717.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199902
EW 19990204
AB Mutational analysis of the promoter region of the ***leptin*** gene in
morbidly obese Finnish subjects had revealed a previously unidentified
C(-188)A polymorphism in the proximal promoter that showed a weak
association with elevated serum ***leptin*** levels in obese male
carriers of the variant (-188A) allele. In this study we demonstrated that
neither expression of reporter gene ***constructs*** driven by
wild-type (-188C) or variant (-188A) proximal promoter regions, nor assay
of binding of cellular proteins reveal a genotype-related difference in
promoter activity.

L29 ANSWER 20 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1998:86832 CAPLUS
DN 128:213111
TI Treatment with CL 316,243, a .beta.3-adrenoceptor agonist, reduces serum
leptin in rats with diet- or aging-associated obesity, but not in
Zucker rats with genetic (fa/fa) obesity
AU Ghorbani, M.; Himms-Hagen, J.
CS Department of Biochemistry, University of Ottawa, Ottawa, ON, K1H 8M5,
Can.
SO Int. J. Obes. (1998), 22(1), 63-65
CODEN: IJOBDP; ISSN: 0307-0565
PB Stockton Press
DT Journal
LA English
AB The effect of chronic treatment with a .beta.3-adrenoceptor agonist, CL
316,243 (CL), on serum ***leptin*** concn. was assessed in rats with
diet-induced obesity (DIO) or with genetic obesity (fa/fa Zucker).
Leptin concn. was measured in serum of young control rats, young
rats with DIO and old control or genetically obese fa/fa Zucker rats, that
were treated chronically with CL for 2-4 wk. Treatment with CL reduced
the elevated ***leptin*** concns. in young rats with DIO and in old
mildly obese control rats to the low concn. of young lean rats. It did
not alter the grossly elevated concn. in fa/fa rats. This effect of CL
correlated well with its previously shown ability to reduce white
adipocyte size, except in fa/fa rats. In CL-treated fa/fa rats,
despite redns. in body fat mass and in white ***adipocyte*** size, and
despite normalization of both hyperglycemia and hyperinsulinemia, the
leptin concn. did not change. The lack of change in
leptin concns. in fa/fa rats, despite shrinking of white
adipocytes and partial reversal of the obesity, may be due to
another defect.

L29 ANSWER 21 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1998:413748 CAPLUS
DN 129:184842
TI Partial cloning and expression of the bovine ***leptin*** gene
AU Ji, Shaoquan; Willis, Gawain M.; Scott, Ronald R.; Spurlock, Michael E.
CS Purina Mills, Inc., St. Louis, MO, USA
SO Anim. Biotechnol. (1998), 9(1), 1-14
CODEN: ANBTEN; ISSN: 1049-5398
PB Marcel Dekker, Inc.
DT Journal
LA English
AB The product of the ***leptin*** (i.e., obese) gene may be an important
regulator of energy metab., adiposity, and reprodn., and is perhaps linked
to meat quality determinants such as marbling. Mol. probes were developed
using polymerase chain reaction (PCR) technol. to evaluate ***leptin***
expression in adipose depots and to evaluate the tissue-dependent nature
of expression reported in other species. A 438 bp fragment representing
the coding region of the bovine ***leptin*** gene excluding the
N-terminal secretory signal was amplified, cloned into a plasmid
vector (pASK75), and expressed in E. coli. Sequence anal. of the
cDNA and the corresponding polypeptide indicate that, overall, both share
approx. 87% homol. with the mouse and human ***leptin*** genes and
polypeptides. Amino terminal sequencing (30 amino acid residues) of the
recombinant bovine ***leptin*** (rBL) protein revealed 100% homol.
with mouse and human ***leptin*** . The bovine ***leptin*** gene
is expressed as a 3090 nt mRNA which is detected in adipose tissue, but is
not found in brain (despite the appreciable fat content and lipid metab.)
or other tissues. ***Leptin*** gene expression in several adipose
depots (s.c., renal, and omental) was similar ($P = .73$) in finished
cattle.

L29 ANSWER 22 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1998:42503 CAPLUS
DN 128:98569
TI Adenoviral mediated gene transfer in ***adipocytes*** and related
implants
IN Crystal, Ronald G.; Magovern, Christopher J.; Rosengart, Todd; Hoffman,
Lloyd; Talmor, Mia
PA Cornell Research Foundation, Inc., USA; Crystal, Ronald G.; Magovern,
Christopher J.; Rosengart, Todd; Hoffman, Lloyd; Talmor, Mia
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9749827	A2	19971231	WO 1997-US11229	19970626

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,

LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG
US 5869037 A 19990209 US 1996-672461 19960626
CA 2259228 AA 19971231 CA 1997-2259228 19970626
AU 9735086 A1 19980114 AU 1997-35086 19970626
EP 914459 A2 19990512 EP 1997-931464 19970626
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE, FI
PRAI US 1996-672461 19960626
WO 1997-US11229 19970626
AB The present invention provides angiogenic factor adenovirus-mediated gene transfer to ***adipocytes*** and, in particular, transfer of toxic genes as a means of reducing adiposity and transfer of genes encoding angiogenic substances to induce new blood vessel growth, as well as adipose tissue implants. The adenoviral ***vector*** is replication-deficient and contains gene regulatory sequences such as a constitutive promoter element, and a gene encoding a protein such as a toxin, angiogenic growth factor, adipsin, or an Ob or ***leptin*** protein. Suitable angiogenic growth factors are the group of vascular endothelial cell growth factors, including VEGF121, VEGF165, or VEGF189. The method can be used to treat energy storage human diseases such as obesity, diabetes, increased body fat deposition, hyperglycemia, hyperinsulinemia, hypothermia, hypertension, hypercholesterolemia, and hyperlipidemia. Angiogeneis is stimulated following adenoviral ***vector*** transfer to and expression in ***adipocytes*** .

L29 ANSWER 23 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1997:785658 CAPLUS
DN 128:84698
TI ***Leptin*** inhibits insulin binding in isolated rat ***adipocytes***
AU Walder, K.; Filippis, A.; Clark, S.; Zimmet, P.; Collier, G. R.
CS Sch. Nutrition & Public Health, Deakin Univ., Geelong, 3217, Australia
SO J. Endocrinol. (1997), 155(3), R5-R7
CODEN: JOENAK; ISSN: 0022-0795
PB Journal of Endocrinology
DT Journal
LA English
AB ***Leptin*** is secreted from adipose tissue, and is thought to act as a 'lipostat', signaling the body fat levels to the hypothalamus resulting in adjustments to food intake and energy expenditure to maintain body wt. homeostasis. In addn., plasma ***leptin*** concns. have been shown to be related to insulin sensitivity independent of body fat content, suggesting that the hyperleptinemia found in obesity could contribute to the insulin resistance. We investigated the effects of ***leptin*** on insulin binding by isolated ***adipocytes*** . ***Adipocytes*** isolated from Sprague-Dawley rats exhibited a dose-dependent redn. in the uptake of 125-labeled insulin when incubated with various concns. of ***exogenous*** ***leptin*** . For example, addn. of 50 nM ***leptin*** reduced total insulin binding in isolated ***adipocytes*** by 19% (P<0.05). Anal. of displacement curve binding data suggested that ***leptin*** reduced maximal insulin binding in a dose-dependent manner, but had no significant effect on the affinity of insulin for its binding site. We conclude that ***leptin*** directly inhibited insulin binding by ***adipocytes*** , and the role of ***leptin*** in the development of insulin resistance in obese individuals requires further investigations.

L29 ANSWER 24 OF 35 MEDLINE DUPLICATE 10
AN 97184189 MEDLINE
DN 97184189
TI Functional antagonism between CCAAT/Enhancer binding protein-alpha and peroxisome proliferator-activated receptor-gamma on the ***leptin*** promoter.
AU Hollenberg A N; Susulic V S; Madura J P; Zhang B; Moller D E; Tontonoz P; Sarraf P; Spiegelman B M; Lowell B B
CS Division of Endocrinology, Beth Israel Hospital, Harvard Medical School, Boston, Massachusetts 02215, USA.
NC DK02119 (NIDDK)
DK49569 (NIDDK)
DK02354 (NIDDK)
+
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Feb 21) 272 (8) 5283-90.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U65742
EM 199706
AB The ***ob*** ***gene*** product, ***leptin*** , is a major hormonal regulator of appetite and fat cell mass. Recent work has suggested that the antidiabetic agents, the thiazolidinediones (TZ), which are also high affinity ligands of peroxisome proliferator-activated receptor-gamma (PPARgamma), inhibit ***leptin*** expression in rodents. To examine the effects of this class of drug on the ***leptin*** gene in ***adipocytes*** we performed Northern analysis on primary rat ***adipocytes*** cultured in the presence or absence of TZ. TZ reduced ***leptin*** mRNA levels by 75%. To determine whether this effect was mediated at the transcriptional level, we isolated 6510 base pairs of 5'-flanking sequence of the ***leptin*** promoter and studied reporter ***constructs*** in primary rat ***adipocytes*** and CV-1 cells. Sequence analysis demonstrated the presence of a consensus direct repeat with a 1-base-pair gap site between -3951 and -3939 as well as a consensus CCAAT/enhancer binding protein (C/EBP) site between -55 and -47. Our functional analysis in transfected primary rat ***adipocytes*** demonstrates that, despite the presence of a canonical direct repeat with a 1-base-pair gap site, TZ alone decreases reporter gene expression of ***leptin*** promoter ***constructs*** ranging from -6510 to +9 to -65 to +9. In CV-1 cells, which contain endogenous PPARgamma, TZ treatment alone had little effect on these ***constructs*** . However, TZ treatment did inhibit C/EBPalpha-mediated transactivation of the ***leptin*** promoter. This down-regulation of ***leptin*** reporter ***constructs*** mapped to a -65 to +9 promoter fragment which binds C/EBPalpha in gel-mobility shift assays but does not bind PPARgamma2 alone or as a heterodimer with 9-cis-retinoic acid receptor. Conversely, the promoter (-5400 to +24 base pairs) of the aP2 gene, another ***adipocyte*** -specific gene, was induced 7.3-fold by TZ. Co-transfection with C/EBPalpha minimally stimulated the aP2 promoter from basal levels but notably blocked activation by TZ. These data indicate

that PPARgamma and C/EBPalpha can functionally antagonize each other on at
least two separate promoters and that this mechanism may explain the
down-regulation of ***leptin*** expression by thiazolidinediones.

L29 ANSWER 25 OF 35 MEDLINE DUPLICATE 11
AN 97272218 MEDLINE
DN 97272218
TI Obese gene expression at in vivo levels by fat pads derived from s.c.
implanted 3T3-F442A preadipocytes [see comments].
CM Comment in: Proc Natl Acad Sci U S A 1997 Apr 29;94(9):4242-5
AU Mandrup S; Loftus T M; MacDougald O A; Kuhajda F P; Lane M D
CS Department of Biological Chemistry, Johns Hopkins University School of
Medicine, Baltimore, MD 21205, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
AMERICA, (1997 Apr 29) 94 (9) 4300-5.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199707
AB 3T3-F442A preadipocytes implanted s.c. into athymic mice develop into fat
pads that are indistinguishable from normal adipose tissue. Implanted
preadipocytes harboring a beta-galactosidase transgene gave rise to fat
pads in which almost all ***adipocytes*** expressed
beta-galactosidase. This finding proved that the implanted 3T3-F442A
preadipocytes, rather than endogenous preadipose cells, gave rise to the
newly developed "adipose tissue." 3T3-F442A preadipocytes, when
differentiated into ***adipocytes*** in cell culture, express the
obese gene at an unexpectedly low level, i.e., </=1% the level in adipose
tissue. However, adipose tissue derived from s.c. implanted 3T3-F442A
preadipocytes expressed ***leptin*** mRNA at a level comparable to
that in epididymal adipose tissue. These findings indicate that a
factor(s) or condition, present in the tissue context and necessary for
maximal obese gene expression, is lacking in cell culture. Furthermore,
adipocytes derived from the implanted cells were hormonally
responsive in that ***leptin*** mRNA levels were up-regulated 3- to
8-fold by glucocorticoid injection into the host animal. Thus, these
findings indicate that adipose-specific promoter-reporter
constructs , transfected into 3T3-F442A preadipocytes, can be
tested in an in vivo context during and after development of these cells
into adipose tissue. Furthermore, the effect of transgenes on the
adipogenic development of the implanted preadipocytes can be assessed.
Thus, this approach offers a faster and less costly alternative to the
transgenic mouse method for assessing adipose gene function.

L29 ANSWER 26 OF 35 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97054688 EMBASE
DN 1997054688
TI ***Leptin*** receptor (OB-R) signaling. Cytoplasmic domain mutational
analysis and evidence for receptor homo-oligomerization.
AU White D.W.; Kuropatwinski K.K.; Devos R.; Baumann H.; Tartaglia L.A.
CS H. Baumann, Dept. of Molecular/Cellular Biology, Roswell Park Cancer
Institute, Elm and Carlton Sts., Buffalo, NY 14263, United States
SO Journal of Biological Chemistry, (1997) 272/7 (4065-4071).
Refs: 41
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 029 Clinical Biochemistry
LA English
SL English
AB The ***leptin*** receptor (OB-K) mediates the weight regulatory
effects of the ***adipocyte*** secreted hormone ***leptin*** (OB).
Previously we have shown that the long form of OB-R, expressed
predominantly in the hypothalamus, can mediate ligand-induced activation
of signal transducer and activator of transcription factors 1, 3, and 5
and stimulate transcription via interleukin-6 and hematopoietin receptor
responsive gene elements. Here we report that deletion and tyrosine
substitution mutagenesis of OB-R identifies two distinct regions of the
intracellular domain important for signaling. In addition,
granulocyte-colony stimulatory factor receptor/OB-R and OB-R/granulocyte-
colony stimulatory factor receptor chimeras are signaling competent and
provide evidence that aggregation of two OB-R intracellular domains is
sufficient for ligand-induced receptor activation. However, signaling by
full-length OB-R appears to be relatively resistant to dominant negative
repression by signaling-incompetent OB-R, suggesting that mechanisms exist
to permit signaling by the long form of OB-R even in the pretence of
excess naturally occurring short form of OB-R.

L29 ANSWER 27 OF 35 MEDLINE
AN 97474783 MEDLINE
DN 97474783
TI Elevated levels of SREBP-2 and cholesterol synthesis in livers of mice
homozygous for a targeted disruption of the SREBP-1 gene [see comments].
CM Comment in: J Clin Invest 1997 Oct 15;100(8):1905-6
AU Shimano H; Shimomura I; Hammer R E; Herz J; Goldstein J L; Brown M S;
Horton J D
CS Department of Molecular Genetics, University of Texas Southwestern Medical
Center, Dallas, Texas 75235, USA.
NC HL-20948 (NHLBI)
SO JOURNAL OF CLINICAL INVESTIGATION, (1997 Oct 15) 100 (8) 2115-24.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199801
EW 19980104
AB The synthesis of cholesterol and its uptake from plasma LDL are regulated
by two membrane-bound transcription factors, designated sterol regulatory
element binding protein-1 and -2 (SREBP-1 and SREBP-2). Here, we used the
technique of homologous recombination to generate mice with disruptions in
the gene encoding the two isoforms of SREBP-1, termed SREBP-1a and
SREBP-1c. Heterozygous gene-disrupted mice were phenotypically normal, but
50- 85% of the homozygous (-/-) mice died in utero at embryonic day 11.
The surviving -/- mice appeared normal at birth and throughout life. Their
livers expressed no functional SREBP-1. There was a 1.5-fold upregulation
of SREBP-2 at the level of mRNA and a two- to threefold increase in the
amount of mature SREBP-2 in liver nuclei. Previous studies showed that
SREBP-2 is much more potent than SREBP-1c, the predominant hepatic isoform
of SREBP-1, in activating transcription of genes encoding enzymes of

cholesterol synthesis. Consistent with this observation, the SREBP-1 -/-
animals manifested elevated levels of mRNAs for 3-hydroxy-3-methylglutaryl
coenzyme A synthase and reductase, farnesyl diphosphate synthase, and
squalene synthase. Cholesterol synthesis, as measured by the incorporation
of [3H]water, was elevated threefold in livers of the -/- mice, and
hepatic cholesterol content was increased by 50%. Fatty acid synthesis was
decreased in livers of the -/- mice. The amount of white adipose tissue
was not significantly decreased, and the levels of mRNAs for lipogenic
enzymes, ***adipocyte*** lipid binding protein, lipoprotein lipase,
and ***leptin*** were normal in the -/- mice. We conclude from these
studies that SREBP-2 can replace SREBP-1 in regulating cholesterol
synthesis in livers of mice and that the higher potency of SREBP-2
relative to SREBP-1c leads to excessive hepatic cholesterol synthesis in
these animals.

L29 ANSWER 28 OF 35 MEDLINE DUPLICATE 12
AN 97344143 MEDLINE
DN 97344143
TI Beta-3 adrenoceptor (beta-3AR) expression in ***leptin*** treated
OB/OB mice.
AU Breslow M J; An Y; Berkowitz D E
CS The Johns Hopkins Medical Institutions, Department of
Anesthesiology/Critical Care Medicine, Baltimore, Maryland 21287-8711,
USA.. mbreslow@welchlink.welch.jhu.edu
SO LIFE SCIENCES, (1997) 61 (1) 59-64.
Journal code: L62. ISSN: 0024-3205.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199709
EW 19970904
AB ***Leptin*** -deficient Ob/Ob mice are hypometabolic and have reduced
fat cell expression of beta-3 adrenoceptors (ARs). To determine whether
leptin repletion restores beta-3 AR number, C57BL/6J Ob/Ob mice
were given ***exogenous*** ***leptin*** (5 mg/kg I.P. daily) for
21 days. ***Leptin*** administration reduced body weight from
43.1+/-3.7 to 34.1+/-3.7 g in Ob/Ob animals but had no effect on weight in
wildtype animals. Body weight increased by 12% in Ob/Ob mice receiving
saline. Beta-3 AR mRNA concentrations were markedly reduced in Ob/Ob
animals at baseline. ***Leptin*** increased beta-3 AR mRNA to control
levels in Ob/Ob mice, but had no effect in wildtype animals.
Adipocyte ***leptin*** mRNA was increased by 400% in Ob/Ob
mice and did not suppress with ***exogenous*** ***leptin***
administration, suggesting no direct feedback regulation of ***leptin***
synthesis. We speculate that restoration of beta-3 AR expression by
repleting ***leptin*** may be important in correcting hypometabolism
in Ob/Ob animals.

L29 ANSWER 29 OF 35 MEDLINE DUPLICATE 13
AN 1998148986 MEDLINE
DN 98148986
TI ***Leptin*** inhibits insulin binding in isolated rat ***adipocytes*** .
AU Walder K; Filippis A; Clark S; Zimmet P; Collier G R
CS School of Nutrition & Public Health, Deakin University, Geelong,
Australia.
SO JOURNAL OF ENDOCRINOLOGY, (1997 Dec) 155 (3) R5-7.
Journal code: I1J. ISSN: 0022-0795.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199805
EW 19980502
AB ***Leptin*** is secreted from adipose tissue, and is thought to act as
a 'lipostat', signalling the body fat levels to the hypothalamus resulting
in adjustments to food intake and energy expenditure to maintain body
weight homeostasis. In addition, plasma ***leptin*** concentrations
have been shown to be related to insulin sensitivity independent of body
fat content, suggesting that the hyperleptinemia found in obesity could
contribute to the insulin resistance. We investigated the effects of
leptin on insulin binding by isolated ***adipocytes***
. ***Adipocytes*** isolated from Sprague-Dawley rats exhibited a
dose-dependent reduction in the uptake of 125I-labelled insulin when
incubated with various concentrations of ***exogenous***
leptin . For example, addition of 50 nM ***leptin*** reduced
total insulin binding in isolated ***adipocytes*** by 19% (P < 0.05).
Analysis of displacement curve binding data suggested that ***leptin***
reduced maximal insulin binding in a dose-dependent manner, but had no
significant effect on the affinity of insulin for its binding site. We
conclude that ***leptin*** directly inhibited insulin binding by
adipocytes , and the role of ***leptin*** in the development of
insulin resistance in obese individuals requires further investigation.

L29 ANSWER 30 OF 35 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97380834 EMBASE
DN 1997380834
TI ***Leptin*** inhibits insulin binding in isolated rat ***adipocytes*** .
AU Walder K.; Filippis A.; Clark S.; Zimmet P.; Collier G.R.
CS G.R. Collier, Sch. of Nutrition and Public Health, Deakin University,
Geelong 3217, Australia
SO Journal of Endocrinology, (1997) 155/3 (R5-R7).
Refs: 13
ISSN: 0022-0795 CODEN: JOENAK
CY United Kingdom
DT Journal; Article
FS 003 Endocrinology
LA English
SL English
AB ***Leptin*** is secreted from adipose tissue, and is thought to act as
a 'lipostat', signalling the body fat levels to the hypothalamus resulting
in adjustments to food intake and energy expenditure to maintain body
weight homeostasis. In addition, plasma ***leptin*** concentrations
have been shown to be related to insulin sensitivity independent of body
fat content, suggesting that the hyperleptinemia found in obesity could
contribute to the insulin resistance. We investigated the effects of
leptin on insulin binding by isolated ***adipocytes***
. ***Adipocytes*** isolated from Sprague-Dawley rats exhibited a
dose-dependent reduction in the uptake of 125I-labelled insulin when
incubated with various concentrations of ***exogenous***
leptin . For example, addition of 150 nM ***leptin*** reduced
total insulin binding in isolated ***adipocytes*** by 19% (P<0.05).
Analysis of displacement curve binding data suggested that

leptin
reduced maximal insulin binding in a dose- dependent manner, but had no
significant effect on the affinity of insulin for its binding site. We conclude that ***leptin*** directly inhibited insulin binding by ***adipocytes*** , and the role of ***leptin*** in the development of
insulin resistance in obese individuals requires further investigation.

L29 ANSWER 31 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1996:701935 CAPLUS
DN 126:2513
TI Anti-obesity proteins
IN Basinski, Margret B.; Dimarchi, Richard D.; Flora, David B.; Heath,
William F., Jr.; Hoffmann, James A.; Schoner, Brigitte E.; Shields, James
E.; Smiley, David L.
PA Eli Lilly and Company, USA
SO U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 381, 247.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5569744	A	19961029	US 1995-383632	19950206
WO 9623514	A1	19960808	WO 1996-US947	19960129
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2211656	AA	19960808	CA 1996-2211656	19960129
AU 9647660	A1	19960821	AU 1996-47660	19960129
AU 9647659	A1	19960821	AU 1996-47659	19960129
EP 836620	A1	19980422	EP 1996-903648	19960129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				
JP 11501297	T2	19990202	JP 1996-523609	19960129
PRAI US 1995-381247	19950131			
US 1995-381034	19950131			
US 1995-381037	19950131			
US 1995-381040	19950131			
US 1995-381041	19950131			
US 1995-381047	19950131			
US 1995-381049	19950131			
US 1995-381050	19950131			
US 1995-381054	19950131			
US 1995-381057	19950131			
US 1995-381163	19950131			
US 1995-381266	19950131			
US 1995-381370	19950131			
US 1995-381451	19950131			
US 1995-381661	19950131			
US 1995-381666	19950131			
US 1995-383492	19950206			
US 1995-383632	19950206			
US 1995-383649	19950206			
US 1995-383650	19950206			
US 1995-384292	19950206			
US 1995-384492	19950206			
US 1995-384649	19950206			
WO 1996-US946	19960129			
WO 1996-US947	19960129			

AB The protein translation product of the obese (ob) mouse gene, and its
amino-acid substitution analogs prepd. by recombinant DNA technol. or
chem. synthesis, are provided as anti-obesity proteins which, when
administered to a patient, regulate fat tissue. The protein may represent
a natural anti-obesity hormone. Such agents allow patients to overcome
their obesity handicap and live normal lives with much reduced risk for
type II diabetes, cardiovascular disease, and cancer. The preferred daily
dose is 10-100 .mu.g protein/kg. Thus, a 141-amino-acid sequence preceded
by Met-Arg was obtained by gene amplification from a human fat cell
library by PCR, insertion into a suitable plasmid ***vector*** ,
cloning, and expression in Escherichia coli K12 RV308.

L29 ANSWER 32 OF 35 CAPLUS COPYRIGHT 1999 ACS
AN 1996:342170 CAPLUS
DN 125:26940
TI Gene ob/ ***leptin*** -related modulators of body weight, corresponding
nucleic acids and proteins, and diagnostic and therapeutic uses thereof
IN Friedman, Jeffery M.; Zhang, Yiying; Proenca, Ricardo; Maffei, Margherita;
Halaas, Jeffrey L.; Gajiwala, Ketan; Burley, Stephen K.
PA Rockefeller University, USA
SO Brit. UK Pat. Appl., 304 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2292382	A1	19960221	GB 1995-16947	19950817
GB 2292382	B2	19970716		
US 5935810	A	19990810	US 1994-347563	19941130
PRAI US 1994-292345	19940817			
US 1994-347563	19941130			
US 1995-438431	19950510			
US 1995-483211	19950607			

AB Polypeptides, which modulate obesity, of ca. 167 amino acids, of human and
murine origin are disclosed, together with allelic variants and fragments
thereof, having identical biol. activity. There are also disclosed
nucleic acid sequences which encode the polypeptides, which may be
inserted into a ***vector*** , either for cloning, or for expression in
a bacterial, insect, fungal (esp. yeast) plant, or mammalian, host.
Oligonucleotides for use either as probes or as primers for PCR
amplification are disclosed. Antibodies (either monoclonal or polyclonal)
are provided. The polypeptides may be conjugated with water-sol.
polymers, esp. polyethyleneglycol. The polypeptides, or antagonists
(including the antibodies) thereto, may be formulated for the control of
body wt. The polypeptides, optionally in combination with a second
component, are of use in the treatment of diabetes, high blood pressure
and high cholesterol levels. Nucleic acid sequences, encoding the
polypeptides, are of use in gene therapy for modulation of body wt., while
sequences, hybridizable thereto, may be formulated for the same purpose.
In vitro methods of evaluation (including detection and diagnosis) of
levels of the OB polypeptide, including monitoring of therapeutic
treatment, are also disclosed. Mouse and human ***leptin*** cDNA and
the human ***leptin*** -encoding ***ob*** ***gene*** were
cloned and sequenced. The human ***ob*** ***gene*** was mapped to
chromosome 7. Eight microsatellite markers in close proximity to this
gene were identified. Synthetic genes for mouse and human ***leptin***
with Escherichia coli-optimized codons were prepd. and expressed in E.
coli. ***Leptin*** , a hormone produced by ***adipocytes*** , was
found to circulate in the blood. ***Leptin*** was absent from plasma
of ob/ob mice. Daily injection of recombinant ***leptin*** dramatically reduced the body mass of ob/ob mice and significantly affected body wt. of wild-type mice.

L29 ANSWER 33 OF 35 MEDLINE DUPLICATE

14
AN 96214975 MEDLINE
DN 96214975
TI Regulation of expression of ob mRNA and protein by glucocorticoids and
cAMP.
AU Slieker L J; Sloop K W; Surface P L; Kriauciunas A; LaQuier F; Manetta J;
Bue-Valleskey J; Stephens T W
CS Endocrine Research and Technology Core Divisions, Lilly Research
Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46285, USA.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Mar 8) 271 (10) 5301-4.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199608
AB Regulation of obese gene (ob) expression in ob/ob and db/db mice and in
cultured rat ***adipocytes*** was examined. It has been demonstrated
that ***exogenous*** human OB protein (***leptin***) treatment
reduces food intake and weight gain, as well as insulin, glucose, and
corticosterone levels in ob/ob mice. In the present report we show that
leptin treatment down-regulates endogenous adipose ob mRNA.
However, treatment of isolated rat ***adipocytes*** with 100 ng/ml
human or murine ***leptin*** had no direct effect on expression of
endogenous ob mRNA, suggesting that ***leptin*** may be able to
down-regulate its own expression by an indirect, non-autocrine mechanism.
Glucocorticoids increased both ob mRNA levels and secreted ***leptin***
levels in vitro. Conversely, agents that increase intracellular cAMP, such
as beta-adrenergic agonists or Bt2cAMP itself, decreased ob mRNA
expression and ***leptin*** secretion. Therefore, increased
glucocorticoid levels and decreased sympathetic neural activity may
contribute to the elevated ob mRNA expression observed in genetically
obese, hyperglucocorticoid rodents. Furthermore, ***leptin*** might
regulate its own expression through a feedback mechanism involving the
hypothalamic pituitary axis.

L29 ANSWER 34 OF 35 MEDLINE DUPLICATE

15
AN 96210599 MEDLINE
DN 96210599
TI Identification of the promoter of the mouse obese gene.
AU de la Brousse F C; Shan B; Chen J L
CS Tularik Inc., South San Francisco, CA 94080, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
AMERICA, (1996 Apr 30) 93 (9) 4096-101.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U52147
EM 199609
AB Primer extension and RACE (rapid amplification of cDNA ends) assays were
used to identify and sequence the 5' terminus of mouse ob mRNA. This
sequence was used to obtain a recombinant bacteriophage containing the
first exon of the encoding gene. DNA sequence analysis of the region
immediately upstream of the first exon of the mouse ***ob***
gene revealed DNA sequences corresponding to presumptive
cis-regulatory elements. A canonical TATA box was observed 30-34 base
pairs upstream from the start site of transcription and a putative binding
site for members of the C/EBP family of transcription factors was
identified immediately upstream from the TATA box. Nuclear extracts
prepared from primary ***adipocytes*** contained a DNA binding
activity capable of avid and specific interaction with the putative C/EBP
response element; antibodies to C/EBP alpha neutralized the DNA binding
activity present in ***adipocyte*** nuclear extracts. When linked to a
firefly luciferase reporter and transfected into primary
adipocytes , the presumptive promoter of the mouse ***ob***
gene facilitated luciferase expression. When transfected into
HepG2 cells, which lack C/EBP alpha, the mouse ob promoter was only weakly
active. Supplementation of C/EBP alpha by cotransfection with a C/EBP
alpha expression ***vector*** markedly stimulated luciferase
expression. Finally, an ob promoter variant mutated at the C/EBP response
element was inactive in both primary ***adipocytes*** and HepG2 cells.
These observations provide evidence for identification of a functional
promoter capable of directing expression of the mouse ***ob***
gene .

L29 ANSWER 35 OF 35 MEDLINE DUPLICATE

16
AN 96149401 MEDLINE
DN 96149401
TI Transcriptional activation of the mouse obese (***ob***) ***gene***
by CCAAT/enhancer binding protein alpha.
AU Hwang C S; Mandrup S; MacDougald O A; Geiman D E; Lane M D
CS Department of Biological Chemistry, Johns Hopkins University School of
Medicine, Baltimore, MD 21205, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
AMERICA, (1996 Jan 23) 93 (2) 873-7.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-S81087
EM 199605
AB Like other ***adipocyte*** genes that are transcriptionally activated
by CCAAT/enhancer binding protein alpha (C/EBP alpha) during preadipocyte
differentiation, expression of the mouse obese (***ob***) ***gene***
is immediately preceded by the expression of C/EBP alpha. While the 5'
flanking region of the mouse ***ob*** ***gene*** contains several
consensus C/EBP binding sites, only one of these sites appears to be
functional. DNase I cleavage inhibition patterns (footprinting) of the
ob ***gene*** promoter revealed that recombinant C/EBP alpha,
as well as a nuclear factor present in fully differentiated 3T3-L1
adipocytes , but present at a much lower level in preadipocytes,
protects the same region between nucleotides -58 and -42 relative to the
transcriptional start site. Electrophoretic mobility-shift analysis using
nuclear extracts from adipose tissue or 3T3-L1 ***adipocytes*** and an
oligonucleotide probe corresponding to a consensus C/EBP binding site at
nucleotides -55 to -47 generated a specific protein-oligonucleotide
complex that was supershifted by antibody against C/EBP alpha. Probes
corresponding to two upstream consensus C/EBP binding sites

failed to
generate protein-oligonucleotide complexes. Cotransfection of a C/EBP
alpha expression ***vector*** into 3T3-L1 cells with a series of 5'
truncated ***ob*** ***gene*** promoter ***constructs***
activated reporter gene expression with all ***constructs***
containing the proximal C/EBP binding site (nucleotides -55 to -47).
Mutation of this site blocked transactivation by C/EBP alpha. Taken
together, these findings implicate C/EBP alpha as a transcriptional
activator of the ***ob*** ***gene*** promoter and identify the
functional C/EBP binding site in the promoter.

=> e prockop darwin j/au
E1 9 PROCKOP DARWIN/AU
E2 1 PROCKOP DARWIN D/AU
E3 547 --> PROCKOP DARWIN J/AU
E4 6 PROCKOP DARWIN JOHNSON/AU
E5 1 PROCKOP DARWING J/AU
E6 1 PROCKOP E S/AU
E7 21 PROCKOP L/AU
E8 140 PROCKOP L D/AU
E9 4 PROCKOP LEON/AU
E10 29 PROCKOP LEON D/AU
E11 4 PROCKOP S/AU
E12 1 PROCKOP S A/AU

=> s e3-e4
L30 553 ("PROCKOP DARWIN J"/AU OR "PROCKOP DARWIN JOHNSON"/AU)

=> s l30 and (marrow stroma# or mesenchymal)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L31 18 L30 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI

=> dup rem l31
PROCESSING COMPLETED FOR L31
L32 12 DUP REM L31 (6 DUPLICATES REMOVED)

=> d 1- bib ab
YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

L32 ANSWER 1 OF 12 CAPLUS COPYRIGHT 1999 ACS
AN 1999:565879 CAPLUS
DN 131:179821
TI Isolated stromal cells for use in the treatment of diseases of the central
nervous system
IN ***Prockop, Darwin J.*** ; Stokes, David G.; Azizi, S. Ausim; Phinney, Donald G.
PA MCP Hahnemann University, USA
SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
---------- ---- -------- ---------- --------
PI WO 9943286 A2 19990902 WO 1999-US3897 19990224
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-28395 19980224
AB Methods of treating a human patient having a disease, disorder or condition of the central nervous system are disclosed. The methods include obtaining a bone marrow sample from a human donor, isolating
stromal cells from the bone marrow sample, and administering the isolated
stromal cells to the central nervous system of the human patient, wherein
the presence of the isolated stromal cells in the brain effects treatment
of the disease, disorder or condition. Stomal cells which are isolated
may be cultured in vitro, they may be genetically engineered to produce
therapeutic compds., and/or they may be pre-differentiated prior to administration into the central nervous system.

L32 ANSWER 2 OF 12 CAPLUS COPYRIGHT 1999 ACS
AN 1999:616004 CAPLUS
TI ***Marrow*** ***stromal*** cells migrate throughout forebrain and
cerebellum, and they differentiate into astrocytes after injection into neonatal mouse brains
AU Kopen, Gene C.; ***Prockop, Darwin J.*** ; Phinney, Donald G.
CS Center for Gene Therapy, MCP Hahnemann University, Philadelphia, PA,
19102-1192, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1999), 96(19), 10711-10716
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Stem cells are a valuable resource for treating disease, but limited access to stem cells from tissues such as brain restricts their utility.
Here, we injected ***marrow*** ***stromal*** cells (MSCs) into the
lateral ventricle of neonatal mice and asked whether these multipotential
mesenchymal progenitors from bone marrow can adopt neural cell
fates when exposed to the brain microenvironment. By 12 days postinjection, MSCs migrated throughout the forebrain and cerebellum
without disruption to the host brain architecture. Some MSCs within the
striatum and the mol. layer of the hippocampus expressed glial fibrillary
acidic protein and, therefore, differentiated into mature astrocytes.
MSCs also populated neuron rich regions including the Islands of Calleja,
the olfactory bulb, and the internal granular layer of the cerebellum. A
large no. of MSCs also were found within the external granular layer of
the cerebellum. In addn., neurofilament pos. donor cells were found
within the reticular formation of the brain stem, suggesting that MSCs
also may have differentiated into neurons. Therefore, MSCs are capable of
producing differentiated progeny of a different dermal origin after implantation into neonatal mouse brains. These results suggest that MSCs
are potentially useful as vectors for treating a variety of central nervous system disorders.

L32 ANSWER 3 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
DUPLICATE 1
AN 1999:132732 BIOSIS
DN PREV199900132732
TI Plastic adherent stromal cells from the bone marrow of commonly used
strains of inbred mice: Variation in yield, growth, and differentiation.
AU Phinney, Donnald G. (1); Kopen, Gene; Isaacson, Rivka L.; ***Prockop,***
*** Darwin J.***
CS (1) 10314 New College Build., Mailstgop 421, 245 N. 15th St., Philadelphia, PA 19102 USA
SO Journal of Cellular Biochemistry, (March 15, 1999) Vol. 72, No. 4, pp.

570-585.
ISSN: 0730-2312.
DT Article
LA English
AB Bone ***marrow*** ***stroma*** contains a unique cell population,
referred to as ***marrow*** ***stromal*** cells (MSC5), capable of
differentiating along multiple ***mesenchymal*** cell lineages. A
standard liquid culture system has been developed to isolate MSCs from
whole marrow by their adherence to plastic wherein the cells grow as
clonal populations derived from a single precursor termed the
colony-forming-unit fibroblast (CFU-F). Using this liquid culture system,
we demonstrate that the relative abundance of MSCs in the bone marrow of
five commonly used inbred strains of mice varies as much as 10-fold, and
that the cells also exhibit markedly disparate levels of alkaline
phosphatase expression, an early marker of osteoblast differentiation. For
each strain examined, the method of isolating MSCs by plastic adherence
yields a heterogeneous cell population. These plastic adherent cells also
exhibit widely varying growth kinetics between the different strains.
Importantly, of three inbred strains commonly used to prepare transgenic
mice that we examined, only cells derived from FVB/N marrow readily expand
in culture. Further analysis of cultures derived from FVB/N marrow showed
that most plastic adherent cells express CD11b and CD45, epitopes of
lymphohematopoietic cells. The later consists of both pre-B-cell
progenitors, granulocytic and monocytic precursors, and macrophages.
However, a subpopulation of the MSCs appear to represent bona fide
mesenchymal progenitors, as cells can be induced to differentiate
into osteoblasts and adipocytes after exposure to dexamethasone and into
myoblasts after exposure to amphotericin B. Our results point to
significant strain differences in the properties of MSCs and indicate that
standard methods cannot be applied to murine bone marrow to isolate
relatively pure populations of MSCs.

L32 ANSWER 4 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1999:159793 BIOSIS
DN PREV199900159793
TI Transplantability and therapeutic effects of bone marrow-derived
mesenchymal cells in children with osteogenesis imperfecta.
AU Horwitz, Edwin M. (1); ***Prockop, Darwin J.*** ; Fitzpatrick, Lorraine
A.; Koo, Winston W. K.; Gordon, Patricia L. (1); Neel, Michael (1);
Sussman, Michael; Orchard, Paul; Marx, Jeffrey C.; Pyeritz, Reed E.;
Brenner, Malcolm K. (1)
CS (1) Cell and Gene Therapy Program, St. Jude Children's Research Hosp., 332
North Lauderdale, Memphis, TN 38105 USA
SO Nature Medicine, (March, 1999) Vol. 5, No. 3, pp. 309-313.
ISSN: 1078-8956.
DT Article
LA English
AB In principle, transplantation of ***mesenchymal*** progenitor cells
would attenuate or possibly correct genetic disorders of bone, cartilage
and muscle, but clinical support for this concept is lacking. Here we
describe the initial results of allogeneic bone marrow transplantation in
three children with osteogenesis imperfecta, a genetic disorder in which
osteoblasts produce defective type I collagen, leading to osteopenia,
multiple fractures, severe bony deformities and considerably shortened
stature. Three months after osteoblast engraftment (1.5-2.0% donor cells),
representative specimens of trabecular bone showed histologic changes
indicative of new dense bone formation. All patients had increases in
total body bone mineral content ranging from 21 to 29 grams (median, 28),
compared with predicted values of 0 to 4 grams (median, 0) for healthy
children with similar changes in weight. These improvements were
associated with increases in growth velocity and reduced frequencies of
bone fracture. Thus, allogeneic bone marrow transplantation can lead to
engraftment of functional ***mesenchymal*** progenitor cells,
indicating the feasibility of this strategy in the treatment of
osteogenesis imperfecta and perhaps other ***mesenchymal*** stem cell
disorders as well.

L32 ANSWER 5 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 2
AN 1998:231716 BIOSIS
DN PREV199800231716
TI Engraftment and migration of human bone ***marrow*** ***stromal***
cells implanted in the brains of albino rats-similarities to astrocyte
grafts.
AU Azizi, S. Ausim (1); Stokes, David; Augelli, Brian J.; Digirolamo, Carla;
Prockop, Darwin J.
CS (1) Dep. Neurol., Allegheny Univ. Health Sci., Broad and Vine St., MS 423,
Philadelphia, PA 19102 USA
SO Proceedings of the National Academy of Sciences of the United States of
America, (March 31, 1998) Vol. 95, No. 7, pp. 3908-3913.
ISSN: 0027-8424.
DT Article
LA English
AB Neurotransplantation has been used to explore the development of the
central nervous system and for repair of diseased tissue in conditions
such as Parkinson's disease. Here, we examine the effects of direct
injection into rat brain of human ***marrow*** ***stromal*** cells
(MSCs), a subset of cells from bone marrow that include stem-like
precursors for nonhematopoietic tissues. Human MSCs isolated by their
adherence to plastic were infused into the corpus striatum. Five to 72
days later, brain sections were examined for the presence of the donor
cells. About 20% of the infused cells had engrafted. There was no evidence
of an inflammatory response or rejection. The cells had migrated from the
injection site along known pathways for migration of neural stem cells to
successive layers of the brain. After infusion into the brain, the human
MSCs lost their immunoreactivity to antibodies for collagen I. Initially,
the human cells continued to stain with antibodies to fibronectin but the
region of staining with fibronectin was significantly decreased at 30 and
72 days. The results suggest that MSCs may be useful vehicles for
autotransplantation in both cell and gene therapy for a variety of
diseases of the central nervous system.

L32 ANSWER 6 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 3
AN 1998:132318 BIOSIS
DN PREV199800132318
TI ***Marrow*** ***stromal*** cells as a source of progenitor cells
for nonhematopoietic tissues in transgenic mice with a phenotype of
osteogenesis imperfecta.
AU Pereira, Ruth F.; O'Hara, Michael D.; Laptev, Alexey V.; Halford, Kenneth
W.; Pollard, Marea D.; Class, Reiner; Simon, Daniela; Livezey,

Kristin;
Prockop, Darwin J. (1)
CS (1) Cent. Gene Therapy, Allegheny Univ. Health Sci., 245 N. 15 St., 10118
NCB, Mail Stop 421, Philadelphia, PA 19102-1192 USA
SO Proceedings of the National Academy of Sciences of the United States of
America, (Feb. 3, 1998) Vol. 95, No. 3, pp. 1142-1147.
ISSN: 0027-8424.
DT Article
LA English
AB ***Marrow*** ***stromal*** cells from wild-type mice were infused
into transgenic mice that had a phenotype of fragile bones resembling
osteogenesis imperfecta because they expressed a human minigene for type I
collagen. In mice that were irradiated with potentially lethal levels (700
cGy) or sublethal levels (350 cGy), DNA from the donor ***marrow***
stromal cells was detected consistently in marrow, bone,
cartilage, and lung either 1 or 2.5 mo after the infusions. The DNA also
was detected but less frequently in the spleen, brain, and skin. There
was a small but statistically significant increase in both collagen
content and mineral content of bone 1 mo after the infusion. Similar
results were obtained with infusion of relatively large amounts of
wild-type whole marrow cells into the transgenic mice. In experiments in
which male ***marrow*** ***stromal*** cells were infused into a
female osteogenesis imperfecta-transgenic mouse, fluorescense in situ
hybridization assays for the Y chromosome indicated that, after 2.5 mo,
donor male cells accounted for 4-19% of the fibroblasts or fibroblast-like
cells obtained in primary cultures of the lung, calvaria, cartilage, long
bone, tail, and skin. In a parallel experiment in which whole marrow cells
from a male mouse were infused into a female immunodeficient rag-2 mouse,
donor male cells accounted for 4-6% of the fibroblasts or fibroblast-like
cells in primary cultures. The results support previous suggestions that
marrow ***stromal*** cells or related cells in marrow serve
as a source for continula renewal of cellls or related cells in marrow
serve as a source for continual renewal of cells in a number of
nonhematopoietic tissues.

L32 ANSWER 7 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
DUPLICATE 4
AN 1998:267074 BIOSIS
DN PREV199800267074
TI What holds us together? Why do some of us fall apart? What can we do about
it.
AU ***Prockop, Darwin J. (1)***
CS (1) Cent. Gene Therapy, Allegheny Univ. Health Sciences, 245 N. 15th
Street, Mail Stop 421, Philadelphia, PA USA
SO Matrix Biology, (March, 1998) Vol. 16, No. 9, pp. 519-528.
ISSN: 0945-053X.
DT Article
LA English
AB One of the intriguing questions about complex organisms is, What holds
them together? One of the principal answers is the tough, fibrous material
known as collagen. A related question is, How is collagen made? The
biosynthesis of the protein has several unusual features. One is the
extensive use of the principle of spontaneous self-assembly seen in the
formation of crystals. The three polypeptide chains of the protein fold
into a triple-helical conformation by a process that begins with the
formation of a small nucleus of triple helix at the C-terminus of the
molecule and then propagation of the nucleus in a zipper-like fashion.
Also, the self-assembly of the collagen monomers into fibrils is an
entropy driven, crystallization-like process. Why do some of them fall
apart? Mutations that alter the expression or primary structure of
collagen are the predominant causes of severe skeletal defects such as
osteogenesis imperfecta and chondrodysplasias. Mutations that have milder
effects on the synthesis or structure of the protein are found in a subset
of patients with more common diseases such as osteoporosis and early onset
osteoarthritis. What can we do about the defects in collagen? Recent
results have emphasized the importance of earlier observations that bone
marrow contains a small subset of cells that are progenitors of
osteoblasts, chondroblasts and several other types of nonhematopoietic
cells. After systemic infusion into irradiated mice, the infused cells
slowly replace a small fraction of the cells in bone, cartilage, lung and
several other tissues. Therefore, the results suggest that the cells,
known as ***mesenchymal*** stem cells or ***marrow***
stromal cells, can be used for both cell and gene therapy of
diseases in which bone, cartilage and other connective tissues fall apart.

L32 ANSWER 8 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1999:87279 BIOSIS
DN PREV199900087279
TI A pvuII RFLP at the porcine orosomucoid (ORM) locus.
AU ***Prockop, Darwin J. (1)***
CS (1) Cent. Gene Therapy, Allegheny Univ. Health Sciences, MCP-Hahnemann
Sch. Med., 245 North 15 Street, Mail Stop 421, Philadelphia, PA 19102 USA
SO Journal of Cellular Biochemistry Supplement, (1998) Vol. 0, No. 30-31, pp.
284-285.
ISSN: 0733-1959.
DT Article
LA English

L32 ANSWER 9 OF 12 CAPLUS COPYRIGHT 1999 ACS
AN 1999:47340 CAPLUS
TI ***Marrow*** ***stromal*** cells as stem cells for continual
renewal of nonhematopoietic tissues and as potential vectors for gene
therapy
AU ***Prockop, Darwin J.***
CS Center for Gene Therapy, Allegheny Univ. Health Sci., Hahnemann Sch. Med.,
Philadelphia, PA, 19102, USA
SO J. Cell. Biochem. (1998), (Suppl. 30/31), 284-285
CODEN: JCEBD5; ISSN: 0730-2312
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Unavailable

L32 ANSWER 10 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
DUPLICATE 5
AN 1997:223263 BIOSIS
DN PREV199799514979
TI ***Marrow*** ***stromal*** cells as stem cells for nonhematopoietic tissues.
AU ***Prockop, Darwin J.***
CS Cent. Gene Therapy, Allegheny Univ. Health Sci., MCP-Hahnemann Sch. Med.,
245 North 15th St., Mail Stop 421, Philadelphia, PA 19102 USA
SO Science (Washington D C), (1997) Vol. 276, No. 5309, pp. 71-74.
ISSN: 0036-8075.
DT General Review
LA English
AB ***Marrow*** ***stromal*** cells can be isolated from other cells
in marrow by their tendency to adhere to tissue culture plastic. The cells
have many of the characteristics of stem cells for tissues that can
roughly be defined as ***mesenchymal*** , because they can be
differentiated in culture into osteoblasts, chondrocytes, adipocytes,

and
even myoblasts. Therefore, ***marrow*** ***stromal*** cells
present an intriguing model for examining the differentiation of stem
cells. Also, they have several characteristics that make them potentially
useful for cell and gene therapy.

L32 ANSWER 11 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:46949 BIOSIS
DN PREV199799346152
TI Use of ***marrow*** ***stromal*** cells to replace bone cells in a
transgenic mouse model for osteogenesis imperfecta.
AU Pereira, Ruth F. (1); Halford, Kenneth W. (1); O'Hara, Michael D.;
Pollard, Marea D.; Volpe, Patricia; Laptve, Alexey (1);
Prockop,
*** Darwin J. (1)***
CS (1) Thomas Jefferson Univ., Dep. Biochem., Philadelphia, PA USA
SO Matrix Biology, (1996) Vol. 15, No. 3, pp. 188.
Meeting Info.: Sixth International Conference on the Molecular Biology and
Pathology of Matrix Philadelphia, Pennsylvania, USA June 16-19, 1996
ISSN: 0945-053X.
DT Conference; Abstract
LA English

L32 ANSWER 12 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
DUPLICATE 6
AN 1995:15419 BIOSIS
DN PREV199598029719
TI Type I collagen transgene used as a marker to trace donor ***marrow***
*** stroma*** l cells. Transplanted cells persist up to five months in
bone marrow, spleen, cartilage and lung.
AU Pereira, Ruth F. (1); Halford, Kenneth W.; O'Hara, Michael; Leeper,
Dennis; Pollard, Marea; Sokolov, Boris; ***Prockop, Darwin J.***
CS (1) Dep. Biochem. Mol. Biol., Jefferson Med. Coll., Thoams Jefferson
Univ., Philadelphia, PA 19107 USA
SO Matrix Biology, (1994) Vol. 14, No. 5, pp. 407.
Meeting Info.: Fifth International Conference on the Molecular Biology and
Pathology of Matrix Philadelphia, Pennsylvania, USA June 19-22, 1994
DT Conference
LA English

=> d his

(FILE 'HOME' ENTERED AT 15:12:44 ON 18 OCT 1999)

FILE 'MEDLINE' ENTERED AT 15:12:49 ON 18 OCT 1999
L1 142 S STROMA#(P)(EXOGENOUS GENE OR GENE CONSTRUCT OR VECTOR)/AB,BI
L2 26 S L1 AND PROMOTER#/AB,BI
L3 1 S L2 AND COLLAGEN/AB,BI
L4 14675 S MESENCHYM?/AB,BI
L5 64 S L4(P)(GENE CONSTRUCT OR EXOGENOUS GENE OR VECTOR#)/AB,BI
L6 12 S L5 AND PROMOTER#/AB,BI
L7 443 S STROMAL FIBROBLAST#/AB,BI
L8 11 S L7(P)(VECTOR# OR CONSTRUCT#)/AB,BI
L9 398 S OBESITY GENE OR OBESITY PROTEIN OR OB GENE/AB,BI
L10 1 S L9(10A)(CONSTRUCT OR VECTOR)/AB,BI
L11 0 S OB GENE AND (MESENCHYMAL OR MARROW STROMA# OR STROMAL FIBROBL
L12 69 S LTMC#
L13 0 S L12 AND OB GENE/AB,BI
L14 0 S L12 AND OBESITY FACTOR/AB,BI
L15 9 S OBESITY FACTOR/AB,BI
L16 1867 S LEPTIN/AB,BI
L17 385 S L16 AND ADIPOCYTE#/AB,BI
L18 8138 S ADIPOCYTE#/AB,BI
L19 54 S L18(10A)(CONSTRUCT OR EXOGENOUS OR VECTOR)/AB,BI
L20 1 S L19 AND (OB GENE OR LEPTIN)/AB,BI
L21 14812 S L1 OR L4
L22 0 S L21 AND (OB GENE OR LEPTIN)/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 15:28:51 ON 18
OCT 1999
L23 2 S L22
L24 2 DUP REM L23 (0 DUPLICATES REMOVED)
L25 9655 S OBESITY PROTEIN OR OBESITY FACTOR OR OBESITY GENE OR OB GENE
L26 1681 S L25 AND (STROMA# OR MESENCHYMAL OR ADIPOCYTE#)/AB,BI
L27 363 S L25 AND (CONSTRUCT# OR VECTOR# OR EXOGENOUS)/AB,BI
L28 79 S L27 AND (STROMA# OR MESENCHYMAL OR ADIPOCYTE#)/AB,BI
L29 35 DUP REM L28 (44 DUPLICATES REMOVED)
E PROCKOP DARWIN J/AU
L30 553 S E3-E4
L31 18 S L30 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
L32 12 DUP REM L31 (6 DUPLICATES REMOVED)

=> s l32 and promoter#/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L33 0 L32 AND PROMOTER#/AB,BI

=> e pereira ruth f/au
E1 1 PEREIRA RUSCHEL P/AU
E2 14 PEREIRA RUTH/AU
E3 11 --> PEREIRA RUTH F/AU
E4 1 PEREIRA RUTH FRANCES/AU
E5 1 PEREIRA RUUI FERNANDES/AU
E6 2 PEREIRA RUY J/AU
E7 212 PEREIRA S/AU
E8 18 PEREIRA S A/AU
E9 16 PEREIRA S C/AU
E10 1 PEREIRA S C C/AU
E11 7 PEREIRA S C S/AU
E12 14 PEREIRA S D/AU

=> s e2-e4
L34 26 ("PEREIRA RUTH"/AU OR "PEREIRA RUTH F"/AU OR "PEREIRA RUTH FRANC
ES"/AU)

=> dup rem l34
PROCESSING COMPLETED FOR L34
L35 20 DUP REM L34 (6 DUPLICATES REMOVED)

=> s l35 and (marrow stroma# or mesenchymal)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L36 3 L35 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI

=> dup rem l36
PROCESSING COMPLETED FOR L36
L37 3 DUP REM L36 (0 DUPLICATES REMOVED)

=> d l- bib ab
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L37 ANSWER 1 OF 3 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:132318 BIOSIS
DN PREV199800132318
TI ***Marrow*** ***stromal*** cells as a source of progenitor cells
for nonhematopoietic tissues in transgenic mice with a phenotype of
osteogenesis imperfecta.
AU ***Pereira, Ruth F.*** ; O'Hara, Michael D.; Laptev, Alexey V.;
Halford, Kenneth W.; Pollard, Marea D.; Class, Reiner; Simon, Daniela;
Livezey, Kristin; Prockop, Darwin J. (1)
CS (1) Cent. Gene Therapy, Allegheny Univ. Health Sci., 245 N. 15 St., 10118
NCB, Mail Stop 421, Philadelphia, PA 19102-1192 USA
SO Proceedings of the National Academy of Sciences of the United States of

America, (Feb. 3, 1998) Vol. 95, No. 3, pp. 1142-1147.
ISSN: 0027-8424.
DT Article
LA English
AB ***Marrow*** ***stromal*** cells from wild-type mice were infused
into transgenic mice that had a phenotype of fragile bones resembling
osteogenesis imperfecta because they expressed a human minigene for type I
collagen. In mice that were irradiated with potentially lethal levels (700
cGy) or sublethal levels (350 cGy), DNA from the donor ***marrow***
stromal cells was detected consistently in marrow, bone,
cartilage, and lung either 1 or 2.5 mo after the infusions. The DNA also
was detected but less frequently in the spleen, brain, and skin. There
was a small but statistically significant increase in both collagen
content and mineral content of bone 1 mo after the infusion. Similar
results were obtained with infusion of relatively large amounts of
wild-type whole marrow cells into the transgenic mice. In experiments in
which male ***marrow*** ***stromal*** cells were infused into a
female osteogenesis imperfecta-transgenic mouse, fluorescense in situ
hybridization assays for the Y chromosome indicated that, after 2.5 mo,
donor male cells accounted for 4-19% of the fibroblasts or fibroblast-like
cells obtained in primary cultures of the lung, calvaria, cartilage, long
bone, tail, and skin. In a parallel experiment in which whole marrow cells
from a male mouse were infused into a female immunodeficient rag-2 mouse,
donor male cells accounted for 4-6% of the fibroblasts or fibroblast-like
cells in primary cultures. The results support previous suggestions that
marrow ***stromal*** cells or related cells in marrow serve
as a source for continula renewal of cellls or related cells in marrow
serve as a source for continual renewal of cells in a number of
nonhematopoietic tissues.

L37 ANSWER 2 OF 3 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:46949 BIOSIS
DN PREV199799346152
TI Use of ***marrow*** ***stromal*** cells to replace bone cells in a
transgenic mouse model for osteogenesis imperfecta.
AU ***Pereira, Ruth F. (1)*** ; Halford, Kenneth W. (1); O'Hara, Michael
D.; Pollard, Marea D.; Volpe, Patricia; Laptve, Alexey (1); Prockop,
Darwin J. (1)
CS (1) Thomas Jefferson Univ., Dep. Biochem., Philadelphia, PA USA
SO Matrix Biology, (1996) Vol. 15, No. 3, pp. 188.
Meeting Info.: Sixth International Conference on the Molecular Biology and
Pathology of Matrix Philadelphia, Pennsylvania, USA June 16-19, 1996
ISSN: 0945-053X.
DT Conference; Abstract
LA English

L37 ANSWER 3 OF 3 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:15419 BIOSIS
DN PREV199598029719
TI Type I collagen transgene used as a marker to trace donor ***marrow***
stroma l cells. Transplanted cells persist up to five months in
bone marrow, spleen, cartilage and lung.
AU ***Pereira, Ruth F. (1)*** ; Halford, Kenneth W.; O'Hara, Michael;
Leeper, Dennis; Pollard, Marea; Sokolov, Boris; Prockop, Darwin J.
CS (1) Dep. Biochem. Mol. Biol., Jefferson Med. Coll., Thoams Jefferson
Univ., Philadelphia, PA 19107 USA
SO Matrix Biology, (1994) Vol. 14, No. 5, pp. 407.
Meeting Info.: Fifth International Conference on the Molecular Biology and
Pathology of Matrix Philadelphia, Pennsylvania, USA June 19-22, 1994
DT Conference
LA English

=> e leeper dennis b/au
E1 2 LEEPER DAVID R/AU
E2 6 LEEPER DENNIS/AU
E3 34 --> LEEPER DENNIS B/AU
E4 1 LEEPER DOGULAS A/AU
E5 1 LEEPER DONNA/AU
E6 4 LEEPER DOUGLAS A/AU
E7 29 LEEPER E/AU
E8 1 LEEPER ED/AU
E9 2 LEEPER F/AU
E10 76 LEEPER F J/AU
E11 1 LEEPER FINAN J/AU
E12 1 LEEPER FINIAN/AU

=> s e2-e3
L38 40 ("LEEPER DENNIS"/AU OR "LEEPER DENNIS B"/AU)

=> s l38 and (marrow stroma# or mesenchymal)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L39 2 L38 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI

=> dup rem l39
PROCESSING COMPLETED FOR L39
L40 1 DUP REM L39 (1 DUPLICATE REMOVED)

=> d bib ab

L40 ANSWER 1 OF 1 BIOSIS COPYRIGHT 1999 BIOSIS
DUPLICATE 1
AN 1995:15419 BIOSIS
DN PREV199598029719
TI Type I collagen transgene used as a marker to trace donor ***marrow***
stroma l cells. Transplanted cells persist up to five months in
bone marrow, spleen, cartilage and lung.
AU Pereira, Ruth F. (1); Halford, Kenneth W.; O'Hara, Michael;
Leeper, ***Dennis*** ; Pollard, Marea; Sokolov, Boris; Prockop, Darwin J.
CS (1) Dep. Biochem. Mol. Biol., Jefferson Med. Coll., Thoams Jefferson
Univ., Philadelphia, PA 19107 USA
SO Matrix Biology, (1994) Vol. 14, No. 5, pp. 407.
Meeting Info.: Fifth International Conference on the Molecular Biology and
Pathology of Matrix Philadelphia, Pennsylvania, USA June 19-22, 1994
DT Conference
LA English

=> e o'hara michael d/au
MISMATCHED QUOTE IN EXPAND TERM
MISMATCHED QUOTE IN EXPAND TERM
MISMATCHED QUOTE IN EXPAND TERM
MISMATCHED QUOTE IN EXPAND TERM
MISMATCHED QUOTE IN EXPAND TERM
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting
off or masking.

=> e ohara michael d/au
E1 7 OHARA MEGURU/AU
E2 1 OHARA MICA/AU
E3 0 --> OHARA MICHAEL D/AU
E4 1 OHARA MICHIAKI/AU
E5 1 OHARA MICHIKO/AU
E6 61 OHARA MICHIMASA/AU
E7 6 OHARA MICHINORI/AU
E8 1 OHARA MICHIO/AU

E9 1 OHARA MICHIYA/AU
E10 7 OHARA MIE/AU
E11 1 OHARA MIKIHIKO CENTRAL KOTESAS/AU
E12 52 OHARA MIKIO/AU

=> e kulkosky joseph/au
E1 45 KULKOSKY J/AU
E2 5 KULKOSKY J W/AU
E3 27 --> KULKOSKY JOSEPH/AU
E4 1 KULKOSKY JOSEPH W/AU
E5 1 KULKOSKY JOSEPH WILLIAM/AU
E6 10 KULKOSKY P/AU
E7 155 KULKOSKY P J/AU
E8 1 KULKOSKY P K/AU
E9 1 KULKOSKY P L/AU
E10 2 KULKOSKY PAUL/AU
E11 40 KULKOSKY PAUL J/AU
E12 2 KULKOSKY PETER F/AU

=> s e1-e5
L41 79 ("KULKOSKY J"/AU OR "KULKOSKY J W"/AU OR "KULKOSKY JOSEPH"/AU
OR "KULKOSKY JOSEPH W"/AU OR "KULKOSKY JOSEPH WILLIAM"/AU)

=> s l41 and (marrow stroma# or mesenchymal)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L42 0 L41 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI

=> e phinney donald/au
E1 1 PHINNEY D P/AU
E2 4 PHINNEY DAVID A/AU
E3 3 --> PHINNEY DONALD/AU
E4 22 PHINNEY DONALD G/AU
E5 1 PHINNEY DONALD GEORGE/AU
E6 1 PHINNEY DONNA/AU
E7 1 PHINNEY DONNALD G/AU
E8 8 PHINNEY DOUGLAS/AU
E9 1 PHINNEY DOUGLAS I/AU
E10 5 PHINNEY DOUGLAS L/AU
E11 1 PHINNEY DUANE C/AU
E12 10 PHINNEY E/AU

=> s e3-e5
L43 26 ("PHINNEY DONALD"/AU OR "PHINNEY DONALD G"/AU OR "PHINNEY DONALD
GEORGE"/AU)

=> s l43 and (stroma# or mesenchymal)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L44 7 L43 AND (STROMA# OR MESENCHYMAL)/AB,BI

=> dup rem l44
PROCESSING COMPLETED FOR L44
L45 6 DUP REM L44 (1 DUPLICATE REMOVED)

=> d l- bib ab
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L45 ANSWER 1 OF 6 INPADOC COPYRIGHT 1999
EPODUPLICATE 1

LEVEL 1
AN 113045575 INPADOC ED 19990921 EW 199937 UP 19990921 UW 199937
TI ISOLATED ***STROMAL*** CELLS FOR USE IN THE TREATMENT OF DISEASES OF
THE CENTRAL NERVOUS SYSTEM
IN PROCKOP, DARWIN, J.; STOKES, DAVID, G.; AZIZI, S., AUSIM; PHINNEY,
DONALD, G.
INS PROCKOP DARWIN J; STOKES DAVID G; AZIZI S AUSIM; ***PHINNEY DONALD G***
INA US; US; US; US
PA MCP HAHNEMANN UNIVERSITY; PROCKOP, DARWIN, J.; STOKES, DAVID, G.; AZIZI,
S., AUSIM; PHINNEY, DONALD, G.
PAS MCP HAHNEMANN UNIVERSITY; PROCKOP DARWIN J; STOKES DAVID G; AZIZI S
AUSIM; PHINNEY DONALD G
PAA US; US; US; US; US
TL English; French
LA English
DT Patent
PIT WOA2 PUBL.OF THE INT.APPL. WITHOUT INT.SEARCH REP.
PI WO 9943286 A2 19990902
DS RW: GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE
DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML
MR NE SN TD TG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE
GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US
UZ VN YU ZW
AI WO 1999-US3897 A 19990224
PRAI US 1998-28395 A 19980224
AB Methods of treating a human patient having a disease, disorder or
condition of the central nervous system are disclosed. The methods include obtaining a bone marrow sample from a human donor, isolating
stromal cells from the bone marrow sample, and administering the isolated
stromal cells to the central nervous system of the human patient, wherein
the presence of the isolated stromal cells in the brain effects treatment
of the disease, disorder or condition. Stomal cells which are isolated
may be cultured in vitro, they may be genetically engineered to produce
therapeutic compounds, and/or they may be pre-differentiated prior to
administration into the central nervous system.

L45 ANSWER 2 OF 6 CAPLUS COPYRIGHT 1999 ACS
AN 1999:616004 CAPLUS
TI Marrow ***stromal*** cells migrate throughout forebrain and cerebellum, and they differentiate into astrocytes after injection into neonatal mouse brains
AU Kopen, Gene C.; Prockop, Darwin J.; ***Phinney, Donald G.***
CS Center for Gene Therapy, MCP Hahnemann University, Philadelphia, PA,
19102-1192, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1999), 96(19), 10711-10716
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Stem cells are a valuable resource for treating disease, but limited access to stem cells from tissues such as brain restricts their utility.
Here, we injected marrow ***stromal*** cells (MSCs) into the lateral
ventricle of neonatal mice and asked whether these multipotential
mesenchymal progenitors from bone marrow can adopt neural cell
fates when exposed to the brain microenvironment. By 12 days
postinjection, MSCs migrated throughout the forebrain and cerebellum
without disruption to the host brain architecture. Some MSCs within the
striatum and the mol. layer of the hippocampus expressed glial fibrillary
acidic protein and, therefore, differentiated into mature astrocytes.
MSCs also populated neuron rich regions including the Islands of Calleja,
the olfactory bulb, and the internal granular layer of the cerebellum. A
large no. of MSCs also were found within the external granular layer of
the cerebellum. In addn., neurofilament pos. donor cells were found
within the reticular formation of the brain stem, suggesting that MSCs
also may have differentiated into neurons. Therefore, MSCs are capable of
producing differentiated progeny of a different dermal origin after

implantation into neonatal mouse brains. These results suggest that MSCs
are potentially useful as vectors for treating a variety of central nervous system disorders.

L45 ANSWER 3 OF 6 CAPLUS COPYRIGHT 1999 ACS
AN 1999:103272 CAPLUS
DN 130:265336
TI Plastic adherent ***stromal*** cells from the bone marrow of commonly
used strains of inbred mice: variations in yield, growth, and differentiation
AU ***Phinney, Donald G.*** ; Kopen, Gene; Isaacson, Rivka L.; Prockop,
Darwin J.
CS Center for Gene Therapy, MCP/Hahnemann University, Philadelphia, PA,
19102, USA
SO J. Cell. Biochem. (1999), 72(4), 570-585
CODEN: JCEBD5; ISSN: 0730-2312
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Bone marrow ***stroma*** contains a unique cell population, referred
to as marrow ***stromal*** cells (MSCs), capable of differentiating
along multiple ***mesenchymal*** cell lineages. A std. liq. culture
system has been developed to isolate MSCs from whole marrow by their
adherence to plastic wherein the cells grow as clonal populations derived
from a single precursor termed the colony-forming-unit fibroblast (CFU-F).
Using this liq. culture system, the authors demonstrate that the relative
abundance of MSCs in the bone marrow of five commonly used inbred strains
of mice varies as much as 10-fold, and that the cells also exhibit
markedly disparate levels of alk. phosphatase expression, an early marker
of osteoblast differentiation. For each strain examd., the method of
isolating MSCs by plastic adherence yields a heterogeneous cell
population. These plastic adherent cells also exhibit widely varying
growth kinetics between the different strains. Importantly, of three
inbred strains commonly used to prep. transgenic mice that were examd.,
only cells derived from FVB/N marrow readily expand in culture. Further
anal. of cultures derived from FVB/N marrow showed that most plastic
adherent cells express CD11b and CD45, epitopes of lymphohematopoietic
cells. The later consists of both pre-B-cell progenitors, granulocytic
and monocytic precursors, and macrophages. However, a subpopulation of
the MSCs appear to represent bona fide ***mesenchymal*** progenitors,
as cells can be induced to differentiate into osteoblasts and adipocytes
after exposure to dexamethasone and into myoblasts after exposure to
amphotericin B. The authors' results point to significant strain
differences in the properties of MSCs and indicate that std. methods
cannot be applied to murine bone marrow to isolate relatively pure
populations of MSCs.

L45 ANSWER 4 OF 6 INPADOC COPYRIGHT 1999 EPO

LEVEL 1
AN 26684467 INPADOC EW 199843 UW 199843
TI ISOLATED ***STROMAL*** CELLS AND METHODS OF USING THE SAME
IN PROCKOP, DARWIN, J.; PEREIRA, RUTH, F.; LEEPER, DENNIS, B.; O'HARA,
MICHAEL, D.; KULKOSKY, JOSEPH; PHINNEY, DONALD; LAPTEV, ALEXEY; CARO,
JOSE
INS PROCKOP DARWIN J; PEREIRA RUTH F; LEEPER DENNIS B; O'HARA MICHAEL D;
KULKOSKY JOSEPH; ***PHINNEY DONALD*** ; LAPTEV ALEXEY; CARO JOSE
INA US; US; US; US; US; US; US; US
PA THOMAS JEFFERSON UNIVERSITY
PAS UNIV JEFFERSON
PAA US
TL English; French; German
LA English
DT Patent
PIT EPA1 PUBL. OF APPLICATION WITH SEARCH REPORT
PI EP 871457 A1 19981021
DS R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AI EP 1996-912514 A 19960328
PRAI WO 1996-US4407 W 19960328
US 1995-412066 A 19950328
US 1995-6627 P 19951113

L45 ANSWER 5 OF 6 INPADOC COPYRIGHT 1999 EPO

LEVEL 1
AN 41650743 INPADOC UW 199906
TI ISOLATED ***STROMAL*** CELLS AND METHODS OF USING THE SAME
ISOLATED ***STROMAL*** CELLS AND METHODS OF USING THE SAME
IN PROCKOP, DARWIN, J.; PEREIRA, RUTH, F.; LEEPER, DENNIS, B.; O'HARA,
MICHAEL, D.; KULKOSKY, JOSEPH; PHINNEY, DONALD; LAPTEV, ALEXEY; CARO,
JOSE
INS PROCKOP DARWIN J; PEREIRA RUTH F; LEEPER DENNIS B; O'HARA MICHAEL D;
KULKOSKY JOSEPH; ***PHINNEY DONALD*** ; LAPTEV ALEXEY; CARO JOSE
INA US; US; US; US; US; US; US; US
PA THOMAS JEFFERSON UNIVERSITY; PROCKOP, DARWIN, J.; PEREIRA, RUTH, F.;
LEEPER, DENNIS, B.; O'HARA, MICHAEL, D.; KULKOSKY, JOSEPH; PHINNEY,
DONALD; LAPTEV, ALEXEY; CARO, JOSE
PAS UNIV JEFFERSON; PROCKOP DARWIN J; PEREIRA RUTH F; LEEPER DENNIS B; HARA
MICHAEL D O; KULKOSKY JOSEPH; PHINNEY DONALD; LAPTEV ALEXEY; CARO JOSE
PAA US; US; US; US; US; US; US; US; US
TL English; French
LA English
DT Patent
PIT WOA1 PUBL.OF THE INT.APPL. WITH INT.SEARCH REPORT
PI WO 9630031 A1 19961003
DS RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US US
AI WO 1996-US4407 A 19960328
PRAI US 1995-412066 A2 19950328
US 1995-6627 A2 19951113
OSDW 96-497223

L45 ANSWER 6 OF 6 INPADOC COPYRIGHT 1999 EPO

LEVEL 1
AN 46504721 INPADOC EW 199809 UW 199823
TI ISOLATED ***STROMAL*** CELLS AND METHODS OF USING THE SAME
IN PROCKOP, DARWIN J.; CARO, JOSE; KULKOSKY, JOSEPH; PEREIRA, RUTH F.;
LEEPER, DENNIS B.; PHINNEY, DONALD; LAPTEV, ALEXEY; O'HARA, MICHAEL D.
INS PROCKOP DARWIN J; CARO JOSE; KULKOSKY JOSEPH; PEREIRA RUTH F; LEEPER
DENNIS B; ***PHINNEY DONALD*** ; LAPTEV ALEXEY; O'HARA MICHAEL D
INA US; US; US; US; US; US; US; US
PA THOMAS JEFFERSON UNIVERSITY
PAS UNIV JEFFERSON
PAA US
TL English; French
LA English
DT Patent
PIT CAAA LAID-OPEN APPLICATION
PI CA 2215143 AA 19961003
AI CA 1996-2215143 A 19960328
PRAI US 1995-412066 A 19950328
US 1995-6627 P 19951113
WO 1996-US4407 A 19960326

=> e laptev alexey/au
E1 2 LAPTEV ALEXANDR GRIGORIEVICH/AU
E2 2 LAPTEV ALEXEI V/AU
E3 5 --> LAPTEV ALEXEY/AU
E4 6 LAPTEV ALEXEY V/AU
E5 2 LAPTEV ANATOLIJ/AU
E6 1 LAPTEV ANATOLIJ A/AU
E7 6 LAPTEV ANATOLIJ B/AU
E8 1 LAPTEV ANATOLIJ E/AU
E9 4 LAPTEV ANATOLIJ F/AU
E10 29 LAPTEV ANATOLIJ G/AU
E11 2 LAPTEV ANATOLIJ GRIGOREVICH/AU
E12 11 LAPTEV ANATOLIJ I/AU

=> s e1-e4
L46 15 ("LAPTEV ALEXANDR GRIGORIEVICH"/AU OR "LAPTEV ALEXEI V"/AU OR "LAPTEV ALEXEY"/AU OR "LAPTEV ALEXEY V"/AU)

=> s l46 and (stroma# or mesenchymal)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L47 5 L46 AND (STROMA# OR MESENCHYMAL)/AB,BI

=> dup rem l47
PROCESSING COMPLETED FOR L47
L48 4 DUP REM L47 (1 DUPLICATE REMOVED)

=> d 1- bib ab
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L48 ANSWER 1 OF 4 INPADOC COPYRIGHT 1999 EPO

LEVEL 1
AN 26684467 INPADOC EW 199843 UW 199843
TI ISOLATED ***STROMAL*** CELLS AND METHODS OF USING THE SAME
IN PROCKOP, DARWIN, J.; PEREIRA, RUTH, F.; LEEPER, DENNIS, B.; O'HARA, MICHAEL, D.; KULKOSKY, JOSEPH; PHINNEY, DONALD; LAPTEV, ALEXEY; CARO, JOSE
INS PROCKOP DARWIN J; PEREIRA RUTH F; LEEPER DENNIS B; O'HARA MICHAEL D; KULKOSKY JOSEPH; PHINNEY DONALD; ***LAPTEV ALEXEY*** ; CARO JOSE
INA US; US; US; US; US; US; US; US
PA THOMAS JEFFERSON UNIVERSITY
PAS UNIV JEFFERSON
PAA US
TL English; French; German
LA English
DT Patent
PIT EPA1 PUBL. OF APPLICATION WITH SEARCH REPORT
PI EP 871457 A1 19981021
DS R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
AI EP 1996-912514 A 19960328
PRAI WO 1996-US4407 W 19960328
US 1995-412066 A 19950328
US 1995-6627 P 19951113

L48 ANSWER 2 OF 4 BIOSIS COPYRIGHT 1999 BIOSIS
DUPLICATE 1
AN 1998:132318 BIOSIS
DN PREV199800132318
TI Marrow ***stromal*** cells as a source of progenitor cells for nonhematopoietic tissues in transgenic mice with a phenotype of osteogenesis imperfecta.
AU Pereira, Ruth F.; O'Hara, Michael D.; ***Laptev, Alexey V.*** ; Halford, Kenneth W.; Pollard, Marea D.; Class, Reiner; Simon, Daniela; Livezey, Kristin; Prockop, Darwin J. (1)
CS (1) Cent. Gene Therapy, Allegheny Univ. Health Sci., 245 N. 15 St., 10118 NCB, Mail Stop 421, Philadelphia, PA 19102-1192 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (Feb. 3, 1998) Vol. 95, No. 3, pp. 1142-1147. ISSN: 0027-8424.
DT Article
LA English
AB Marrow ***stromal*** cells from wild-type mice were infused into transgenic mice that had a phenotype of fragile bones resembling osteogenesis imperfecta because they expressed a human minigene for type I collagen. In mice that were irradiated with potentially lethal levels (700 cGy) or sublethal levels (350 cGy), DNA from the donor marrow ***stromal*** cells was detected consistently in marrow, bone, cartilage, and lung either 1 or 2.5 mo after the infusions. The DNA also was detected but less frequently in the spleen, brain, and skin. There was a small but statistically significant increase in both collagen content and mineral content of bone 1 mo after the infusion. Similar results were obtained with infusion of relatively large amounts of wild-type whole marrow cells into the transgenic mice. In experiments in which male marrow ***stromal*** cells were infused into a female osteogenesis imperfecta-transgenic mouse, fluorescense in situ hybridization assays for the Y chromosome indicated that, after 2.5 mo, donor male cells accounted for 4-19% of the fibroblasts or fibroblast-like cells obtained in primary cultures of the lung, calvaria, cartilage, long bone, tail, and skin. In a parallel experiment in which whole marrow cells from a male mouse were infused into a female immunodeficient rag-2 mouse, donor male cells accounted for 4-6% of the fibroblasts or fibroblast-like cells in primary cultures. The results support previous suggestions that marrow ***stromal*** cells or related cells in marrow serve as a source for continula renewal of cellls or related cells in marrow serve as a source for continual renewal of cells in a number of nonhematopoietic tissues.

L48 ANSWER 3 OF 4 INPADOC COPYRIGHT 1999 EPO

LEVEL 1
AN 41650743 INPADOC UW 199906
TI ISOLATED ***STROMAL*** CELLS AND METHODS OF USING THE SAME
ISOLATED ***STROMAL*** CELLS AND METHODS OF USING THE SAME
IN PROCKOP, DARWIN, J.; PEREIRA, RUTH, F.; LEEPER, DENNIS, B.; O'HARA, MICHAEL, D.; KULKOSKY, JOSEPH; PHINNEY, DONALD; LAPTEV, ALEXEY; CARO, JOSE
INS PROCKOP DARWIN J; PEREIRA RUTH F; LEEPER DENNIS B; O'HARA MICHAEL D; KULKOSKY JOSEPH; PHINNEY DONALD; ***LAPTEV ALEXEY*** ; CARO JOSE
INA US; US; US; US; US; US; US; US
PA THOMAS JEFFERSON UNIVERSITY; PROCKOP, DARWIN, J.; PEREIRA, RUTH, F.; LEEPER, DENNIS, B.; O'HARA, MICHAEL, D.; KULKOSKY, JOSEPH; PHINNEY, DONALD; LAPTEV, ALEXEY; CARO, JOSE
PAS UNIV JEFFERSON; PROCKOP DARWIN J; PEREIRA RUTH F; LEEPER DENNIS B; HARA MICHAEL D O; KULKOSKY JOSEPH; PHINNEY DONALD; LAPTEV ALEXEY; CARO JOSE
PAA US; US; US; US; US; US; US; US; US
TL English; French
LA English
DT Patent
PIT WOA1 PUBL.OF THE INT.APPL. WITH INT.SEARCH REPORT
PI WO 9630031 A1 19961003
DS RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US US
AI WO 1996-US4407 A 19960328
PRAI US 1995-412066 A2 19950328
US 1995-6627 A2 19951113
OSDW 96-497223

L48 ANSWER 4 OF 4 INPADOC COPYRIGHT 1999 EPO

LEVEL 1
AN 46504721 INPADOC EW 199809 UW 199823
TI ISOLATED ***STROMAL*** CELLS AND METHODS OF USING THE SAME
IN PROCKOP, DARWIN J.; CARO, JOSE; KULKOSKY, JOSEPH; PEREIRA, RUTH F.;
LEEPER, DENNIS B.; PHINNEY, DONALD; LAPTEV, ALEXEY; O'HARA, MICHAEL D.
INS PROCKOP DARWIN J; CARO JOSE; KULKOSKY JOSEPH; PEREIRA RUTH F; LEEPER
DENNIS B; PHINNEY DONALD; ***LAPTEV ALEXEY*** ; O'HARA MICHAEL D
INA US; US; US; US; US; US; US; US
PA THOMAS JEFFERSON UNIVERSITY
PAS UNIV JEFFERSON
PAA US
TL English; French
LA English
DT Patent
PIT CAAA LAID-OPEN APPLICATION
PI CA 2215143 AA 19961003
AI CA 1996-2215143 A 19960328
PRAI US 1995-412066 A 19950328
US 1995-6627 P 19951113
WO 1996-US4407 A 19960326

=> s (stroma#)(10a)(promoter#)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L49 163 (STROMA#)(10A)(PROMOTER#)/AB,BI

=> s l49(10a)(collagen)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L50 4 L49(10A)(COLLAGEN)/AB,BI

=> dup rem l50
PROCESSING COMPLETED FOR L50
L51 1 DUP REM L50 (3 DUPLICATES REMOVED)

=> d bib ab

L51 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
AN 74172340 MEDLINE
DN 74172340
TI Control of corneal differentiation by extracellular materials.
Collagen as a ***promoter*** and stabilizer of epithelial
stroma production.
AU Meier S; Hay E D
SO DEVELOPMENTAL BIOLOGY, (1974 Jun) 38 (2) 249-70.
Journal code: E7T. ISSN: 0012-1606.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 197409

=> s l49(10a)(procollagen or col1a1 or col2a1)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L52 0 L49(10A)(PROCOLLAGEN OR COL1A1 OR COL2A1)/AB,BI

=> s (procollagen or col1a1 or col2a1)(w)(promoter#)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L53 200 (PROCOLLAGEN OR COL1A1 OR COL2A1)(W)(PROMOTER#)/AB,BI

=> s l53(p)(obesity gene or ob gene or obesity protein or leptin)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L54 0 L53(P)(OBESITY GENE OR OB GENE OR OBESITY PROTEIN OR LEPTIN)/AB
,BI

=> s l53(10a)(stroma# or mesenchymal)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L55 0 L53(10A)(STROMA# OR MESENCHYMAL)/AB,BI

=> s l53(10a)(marrow)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L56 0 L53(10A)(MARROW)/AB,BI

=> s l53(p)(stroma# or mesenchymal)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L57 4 L53(P)(STROMA# OR MESENCHYMAL)/AB,BI

=> dup rem l57
PROCESSING COMPLETED FOR L57
L58 1 DUP REM L57 (3 DUPLICATES REMOVED)

=> d bib ab

L58 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
AN 96066708 MEDLINE
DN 96066708
TI Stimulation of alpha 1 (I) procollagen gene expression in NIH-3T3 cells by
the human T cell leukemia virus type 1 (HTLV-1) Tax gene.
AU Munoz E; Suri D; Amini S; Khalili K; Jimenez S A
CS Department of Medicine, Jefferson Medical College, Thomas Jefferson
University, Philadelphia, Pennsylvania 19107, USA..
NC AM-19616 (NIADDK)
AI-28272 (NIAID)
SO JOURNAL OF CLINICAL INVESTIGATION, (1995 Nov) 96 (5) 2413-20.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199602
AB The mechanisms that regulate the expression of genes encoding
extracellular matrix proteins in fibroblasts and other ***mesenchymal***
cells have remained elusive. Studies from several laboratories have
indicated that Tax, a trans-regulatory protein from the human T cell
leukemia virus type I not only augments viral gene expression but also
triggers the expression of various cellular genes. Here, we examined the
hypothesis that the expression of collagen genes may also be modulated by
Tax. NIH-3T3 cells were simultaneously transfected with a Tax expressor
plasmid and a chimeric construct containing regulatory sequences (-804 to
+42 bp) of the alpha 1(I) procollagen gene (***COL1A1*** ***promoter*** . The results indicated that the promoter activity of the
-804 to bp COL1A1 fragment increased up to 12-fold in cells expressing
Tax. Deletion analysis revealed that the region of COL1A1 encompassing
nucleotides -174 to -84 contained the Tax-responsive elements. A gene
segment encompassing nucleotides -187 to -67, which contained this region,
proved sufficient to confer Tax inducibility (2.5-fold) to a herpes
simplex virus thymidine kinase promoter. Stably transfected NIH-3T3 cell
clones that constitutively produce Tax displayed elevated levels of alpha
1(I) procollagen and fibronectin transcripts and increased

production and
accelerated processing of type I procollagen. These findings suggest that
retroviral proteins may be involved in the pathogenesis of idiopathic
diseases accompanied by collagen overproduction.

=> d his

(FILE 'HOME' ENTERED AT 15:12:44 ON 18 OCT 1999)

FILE 'MEDLINE' ENTERED AT 15:12:49 ON 18 OCT 1999
L1 142 S STROMA#(P)(EXOGENOUS GENE OR GENE CONSTRUCT OR VECTOR)/AB,BI
L2 26 S L1 AND PROMOTER#/AB,BI
L3 1 S L2 AND COLLAGEN/AB,BI
L4 14675 S MESENCHYM?/AB,BI
L5 64 S L4(P)(GENE CONSTRUCT OR EXOGENOUS GENE OR VECTOR#)/AB,BI
L6 12 S L5 AND PROMOTER#/AB,BI
L7 443 S STROMAL FIBROBLAST#/AB,BI
L8 11 S L7(P)(VECTOR# OR CONSTRUCT#)/AB,BI
L9 398 S OBESITY GENE OR OBESITY PROTEIN OR OB GENE/AB,BI
L10 1 S L9(10A)(CONSTRUCT OR VECTOR)/AB,BI
L11 0 S OB GENE AND (MESENCHYMAL OR MARROW STROMA# OR STROMAL FIBROBL
L12 69 S LTMC#
L13 0 S L12 AND OB GENE/AB,BI
L14 0 S L12 AND OBESITY FACTOR/AB,BI
L15 9 S OBESITY FACTOR/AB,BI
L16 1867 S LEPTIN/AB,BI
L17 385 S L16 AND ADIPOCYTE#/AB,BI
L18 8138 S ADIPOCYTE#/AB,BI
L19 54 S L18(10A)(CONSTRUCT OR EXOGENOUS OR VECTOR)/AB,BI
L20 1 S L19 AND (OB GENE OR LEPTIN)/AB,BI
L21 14812 S L1 OR L4
L22 0 S L21 AND (OB GENE OR LEPTIN)/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 15:28:51 ON 18
OCT 1999
L23 2 S L22
L24 2 DUP REM L23 (0 DUPLICATES REMOVED)
L25 9655 S OBESITY PROTEIN OR OBESITY FACTOR OR OBESITY GENE OR OB GENE
L26 1681 S L25 AND (STROMA# OR MESENCHYMAL OR ADIPOCYTE#)/AB,BI
L27 363 S L25 AND (CONSTRUCT# OR VECTOR# OR EXOGENOUS)/AB,BI
L28 79 S L27 AND (STROMA# OR MESENCHYMAL OR ADIPOCYTE#)/AB,BI
L29 35 DUP REM L28 (44 DUPLICATES REMOVED)
E PROCKOP DARWIN J/AU
L30 553 S E3-E4
L31 18 S L30 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
L32 12 DUP REM L31 (6 DUPLICATES REMOVED)
L33 0 S L32 AND PROMOTER#/AB,BI
E PEREIRA RUTH F/AU
L34 26 S E2-E4
L35 20 DUP REM L34 (6 DUPLICATES REMOVED)
L36 3 S L35 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
L37 3 DUP REM L36 (0 DUPLICATES REMOVED)
E LEEPER DENNIS B/AU
L38 40 S E2-E3
L39 2 S L38 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
L40 1 DUP REM L39 (1 DUPLICATE REMOVED)
E OHARA MICHAEL D/AU
E KULKOSKY JOSEPH/AU
L41 79 S E1-E5
L42 0 S L41 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
E PHINNEY DONALD/AU
L43 26 S E3-E5
L44 7 S L43 AND (STROMA# OR MESENCHYMAL)/AB,BI
L45 6 DUP REM L44 (1 DUPLICATE REMOVED)
E LAPTEV ALEXEY/AU
L46 15 S E1-E4
L47 5 S L46 AND (STROMA# OR MESENCHYMAL)/AB,BI
L48 4 DUP REM L47 (1 DUPLICATE REMOVED)
L49 163 S (STROMA#)(10A)(PROMOTER#)/AB,BI
L50 4 S L49(10A)(COLLAGEN)/AB,BI
L51 1 DUP REM L50 (3 DUPLICATES REMOVED)
L52 0 S L49(10A)(PROCOLLAGEN OR COL1A1 OR COL2A1)/AB,BI
L53 200 S (PROCOLLAGEN OR COL1A1 OR COL2A1)(W)(PROMOTER#)/AB,BI
L54 0 S L53(P)(OBESITY GENE OR OB GENE OR OBESITY PROTEIN OR LEPTIN)
L55 0 S L53(10A)(STROMA# OR MESENCHYMAL)/AB,BI
L56 0 S L53(10A)(MARROW)/AB,BI
L57 4 S L53(P)(STROMA# OR MESENCHYMAL)/AB,BI
L58 1 DUP REM L57 (3 DUPLICATES REMOVED)

=> s l53(p)(bone cell# or osteoblast# or preosteoblast#)/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
2 FILES SEARCHED...
'AB' IS NOT A VALID FIELD CODE
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L59 29 L53(P)(BONE CELL# OR OSTEOBLAST# OR PREOSTEOBLAST#)/AB,BI

=> dup rem l59
PROCESSING COMPLETED FOR L59
L60 8 DUP REM L59 (21 DUPLICATES REMOVED)

=> d l- bib ab
YOU HAVE REQUESTED DATA FROM 8 ANSWERS -
CONTINUE? Y/(N):y

L60 ANSWER 1 OF 8 MEDLINE DUPLICATE 1
AN 1998241028 MEDLINE
DN 98241028
TI PTH-responsive osteoblast nuclear matrix architectural transcription
factor binds to the rat type I collagen promoter.
AU Alvarez M; Thunyakitpisal P; Morrison P; Onyia J; Hock J; Bidwell J P
CS Department of Oral Biology, Indiana University School of Dentistry,
Indianapolis 46202, USA.
NC R55DK48310 (NIDDK)
RO1 DE07272 (NIDR)
SO JOURNAL OF CELLULAR BIOCHEMISTRY, (1998 Jun 1) 69 (3) 336-52.
Journal code: HNF. ISSN: 0730-2312.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
EW 19980802
AB In connective tissue, cell structure contributes to type I collagen
expression. Differences in ***osteoblast*** microarchitecture may
account for the two distinct cis elements regulating basal expression, in
vivo and in vitro, of the rat type I collagen alpha1(I) polypeptide chain
(COL1A1). The ***COL1A1*** ***promoter*** conformation may be the
penultimate culmination of ***osteoblast*** structure. Architectural
transcription factors bind to the minor groove of AT-rich DNA and bend it,
altering interactions between other trans-acting proteins. Similarly,
nuclear matrix (NM) proteins bind to the minor groove of AT-rich
matrix-attachment regions, regulating transcription by altering DNA
structure. We propose that ***osteoblast*** NM architectural
transcription factors link cell structure to promoter geometry and COL1A1
transcription. Our objective was to identify potential ***osteoblast***
NM architectural transcription factors near the in vitro and in vivo
regulatory regions of the rat ***COL1A1*** ***promoter***. Nuclear
protein-promoter interactions were analyzed by gel shift analysis and
related techniques. NM extracts were derived from rat osteosarcoma cells
and from rat bone. The NM protein, NMP4, and a soluble nuclear protein,
NP, both bound to two homologous poly(dT) elements within the COL1A1 in
vitro regulatory region and proximal to the in vivo regulatory

element.
These proteins bound within the minor groove and bent the DNA. Parathyroid
hormone increased NP/NMP4 binding to both poly(dT) elements and decreased
COL1A1 mRNA in the osteosarcoma cells. NP/NMP4-***COL1A1***
promoter interactions may represent a molecular pathway by which
osteoblast structure is coupled to COL1A1 expression.

L60 ANSWER 2 OF 8 MEDLINE DUPLICATE 2
AN 1998322114 MEDLINE
DN 98322114
TI 1,25-Dihydroxyvitamin D3 inhibition of col1a1 promoter expression in
calvariae from neonatal transgenic mice.
AU Bedalov A; Salvatori R; Dodig M; Kapural B; Pavlin D; Kream B E; Clark S
H; Woody C O; Rowe D W; Lichtler A C
CS Department of Pediatrics, MC1515, University of Connecticut Health Center,
263 Farmington Ave., Farmington, CT 06030, USA.
NC AR29983 (NIAMS)
AR38933 (NIAMS)
AR2985 (NIAMS)
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1998 Jul 9) 1398 (3) 285-93.
Journal code: A0W. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199810
EW 19981004
AB We studied the effect of 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) on organ
cultures of transgenic mouse calvariae containing segments of the
Col1a1 ***promoter*** extending to -3518, -2297, -1997, -1794,
-1763, and -1719 bp upstream of the transcription start site fused to the
chloramphenicol acetyltransferase (CAT) reporter gene. 1,25(OH)2D3 had a
dose-dependent inhibitory effect on the expression of the -3518 bp
promoter construct (ColCAT3.6), with maximal inhibition of about 50% at 10
nM. This level of inhibition was consistent with the previously observed
effect on the endogenous Col1a1 gene in ***bone*** ***cell***
models. All of the shorter constructs were also inhibited by 10 nM
1,25(OH)2D3, suggesting that the sequences required for 1, 25(OH)2D3
inhibition are downstream of -1719 bp. The inhibitory effect of
1,25(OH)2D3 on transgene mRNA was maintained in the presence of the
protein synthesis inhibitor cycloheximide, suggesting that the inhibitory
effect on Col1a1 gene transcription does not require de novo protein
synthesis. We also examined the in vivo effect of 1,25(OH)2D3 treatment of
transgenic mice on ColCAT activity, and found that 48 h treatment caused a
dose-dependent inhibition of CAT activity in calvariae comparable to that
observed in organ cultures. In conclusion, we demonstrated that
1,25(OH)2D3 inhibits ***Col1A1*** ***promoter*** activity in
transgenic mouse calvariae, both in vivo and in vitro. The results
indicate that there is a 1, 25(OH)2D3 responsive element downstream of
-1719 bp. The inhibitory effect does not require new protein synthesis.

L60 ANSWER 3 OF 8 MEDLINE DUPLICATE 3
AN 97131981 MEDLINE
DN 97131981
TI Rat osteoblast and osteosarcoma nuclear matrix proteins bind with sequence
specificity to the rat type I collagen promoter.
AU Alvarez M; Long H; Onyia J; Hock J; Xu W; Bidwell J
CS Department of Oral Biology, Indiana University School of Dentistry,
Indianapolis 46202, USA.
NC R55-DK-48310 (NIDDK)
RO1-DE-07272 (NIDR)
SO ENDOCRINOLOGY, (1997 Jan) 138 (1) 482-9.
Journal code: EGZ. ISSN: 0013-7227.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199703
EW 19970304
AB The nuclear matrix mediates the 3-dimensional organization of DNA and
supports DNA replication and its transcription. We hypothesize that the
osteoblast nuclear matrix contributes to the transcriptional
control of type I collagen (COL1A1) expression. Cis-regulatory elements of
the rat ***COL1A1*** ***promoter*** that control
osteoblast expression in vivo are between -2.3 and -1.67 kilobase
pairs (kb) but lie within -3.5 and -2.3 kb in cultured ***bone***
cells . This may result from differences in cell architecture
between ***osteoblasts*** in tissue and those in vitro. Our aim was to
identify ***osteoblast*** nuclear matrix proteins (NMPs) that
associated with sequence-specificity to the ***COL1A1***
promoter . We used ***osteoblasts*** from the rat metaphyseal
femur and the rat osteosarcoma cells, ROS 17/2.8. Nuclear matrix and
soluble nuclear proteins were obtained as separate subfractions. Gel
mobility shift analysis, using fragments of the ***COL1A1***
promoter , was used to identify DNA-binding proteins in the nuclear
subfractions. A NMP-DNA interaction, NMP3, was observed between -2149 and
-2106 nucleotide in both ***osteoblasts*** and osteosarcoma cells.
NMP4 was detected between -3518 to -3406 nucleotide. Therefore,
osteoblast NMPs recognize sequences in regulatory regions of the
COL1A1 ***promoter*** and may link cell structure and the
transcriptional regulation of this protein.

L60 ANSWER 4 OF 8 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:20020 BIOSIS
DN PREV199800020020
TI The ***osteoblast*** nuclear matrix (NM) protein, NMP4, bends the type
I collagen (***COL1A1***) ***promoter*** .
AU Thunyakiptisal, P.; Alvarez, M.; Morrison, P.; Onyia, J.; Hock, J.;
Bidwell, J. P.
CS Indiana Univ. Sch. Dent., Indianapolis, IN 46202 USA
SO Molecular Biology of the Cell, (Nov., 1997) Vol. 8, No. SUPPL., pp. 102A.
Meeting Info.: 37th Annual Meeting of the American Society for Cell
Biology Washington, D.C., USA December 13-17, 1997 American Society for
Cell Biology
. ISSN: 1059-1524.
DT Conference
LA English

L60 ANSWER 5 OF 8 MEDLINE DUPLICATE 4
AN 96279197 MEDLINE
DN 96279197
TI Identification of a TAAT-containing motif required for high level
expression of the ***COL1A1*** ***promoter*** in differentiated
osteoblasts of transgenic mice.
AU Dodig M; Kronenberg M S; Bedalov A; Kream B E; Gronowicz G; Clark S H;
Mack K; Liu Y H; Maxon R; Pan Z Z; Upholt W B; Rowe D W; Lichtler A C
CS Department of Pediatrics, University of Connecticut Health Center,
Farmington, Connecticut 06030, the Department.
NC AR29983 (NIAMS)
AR38933 (NIAMS)

AR29850 (NIAMS)
+
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Jul 5) 271 (27) 16422-9.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199610
AB Our previous studies have shown that the 49-base pair region of promoter
DNA between -1719 and -1670 base pairs is necessary for transcription of
the rat COL1A1 gene in transgenic mouse calvariae. In this study, we
further define this element to the 13-base pair region between -1683 and
-1670. This element contains a TAAT motif that binds homeodomain-
containing proteins. Site-directed mutagenesis of this element in the
context of a COL1A1-chloramphenicol acetyltransferase construct extending
to -3518 base pairs decreased the ratio of reporter gene activity in
calvariae to tendon from 3:1 to 1:1, suggesting a preferential effect on
activity in calvariae. Moreover, chloramphenicol acetyltransferase-
specific immunofluorescence microscopy of transgenic calvariae showed that
the mutation preferentially reduced levels of chloramphenicol
acetyltransferase protein in differentiated ***osteoblasts*** . Gel
mobility shift assays demonstrate that differentiated ***osteoblasts***
contain a nuclear factor that binds to this site. This binding activity is
not present in undifferentiated ***osteoblasts*** . We show that Msx2,
a homeodomain protein, binds to this motif; however, Northern blot
analysis revealed that Msx2 mRNA is present in undifferentiated
bone ***cells*** but not in fully differentiated
osteoblasts . In addition, cotransfection studies in ROS 17/2.8
osteosarcoma cells using an Msx2 expression vector showed that Msx2
inhibits a ***COL1A1*** ***promoter*** -chloramphenicol
acetyltransferase construct. Our results suggest that high COL1A1
expression in bone is mediated by a protein that is induced during
osteoblast differentiation. This protein may contain a
homeodomain; however, it is distinct from homeodomain proteins reported
previously to be present in bone.

L60 ANSWER 6 OF 8 MEDLINE DUPLICATE 5
AN 95197712 MEDLINE
DN 95197712
TI Analysis of regulatory regions in the COL1A1 gene responsible for
1,25-dihydroxyvitamin D3-mediated transcriptional repression in
osteoblastic cells.
AU Pavlin D; Bedalov A; Kronenberg M S; Kream B E; Rowe D W; Smith C L; Pike
J W; Lichtler A C
CS Department of Orthodontics, University of Texas Health Science Center, San
Antonio 78284..
NC AR29983 (NIAMS)
AR38933 (NIAMS)
AR29850 (NIAMS)
+
SO JOURNAL OF CELLULAR BIOCHEMISTRY, (1994 Dec) 56 (4) 490-501.
Journal code: HNF. ISSN: 0730-2312.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
AB The synthesis of type I collagen in ***bone*** ***cells*** is
inhibited by the calcium-regulating hormone 1,25-dihydroxyvitamin D3.
Earlier work from our laboratories has indicated that vitamin D regulation
is at the level of transcription, based on results from both nuclear
run-off assays and functional promoter analysis of a hybrid gene
consisting of a 3.6 kb ***COL1A1*** ***promoter*** fragment fused
to the chloramphenicol acetyltransferase reporter gene. In the present
study, we investigated the molecular basis for vitamin D-mediated
transcriptional repression of the COL1A1 gene and report the
identification of a region within the COL1A1 upstream promoter (the
HindIII-PstI restriction fragment between nucleotides -2295 and -1670)
which is necessary for 1,25-dihydroxyvitamin D3 responsiveness in
osteoblastic cells. This hormone-mediated inhibitory effect on the marker
gene parallels the inhibition of the endogenous collagen gene. A 41 bp
fragment from this region (between nucleotides -2256 and -2216) contains a
sequence which is very similar to vitamin D-responsive elements identified
in the osteocalcin gene. Extracts from cultured cells which express a high
level of vitamin D receptor contain a hormone:receptor complex that binds
specifically to this 41 bp fragment, as demonstrated by bandshift
analysis. However, deletion of this vitamin D receptor binding region from
either a -3.5 kb or a -2.3 kb promoter fragment did not abolish vitamin D
responsiveness. These results indicate that a vitamin D response element
similar to that described for other vitamin D responsive genes
(osteocalcin and osteopontin) does not alone mediate the repression of
COL1A1 by 1,25-dihydroxyvitamin D3.

L60 ANSWER 7 OF 8 MEDLINE DUPLICATE 6
AN 93360953 MEDLINE
DN 93360953
TI Transgenic expression of COL1A1-chloramphenicol acetyltransferase fusion
genes in bone: differential utilization of promoter elements in vivo and
in cultured cells.
AU Krebsbach P H; Harrison J R; Lichtler A C; Woody C O; Rowe D W; Kream B E
CS Department of Periodontology, University of Connecticut Health Center,
Farmington 06030.
NC AR29983 (NIAMS)
AR29850 (NIAMS)
AR38933 (NIAMS)
+
SO MOLECULAR AND CELLULAR BIOLOGY, (1993 Sep) 13 (9) 5168-74.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199311
AB To directly compare the patterns of collagen promoter expression in cells
and tissues, the activity of COL1A1 fusion genes in calvariae of neonatal
transgenic mice and in primary ***bone*** ***cell*** cultures
derived by sequential digestion of transgenic calvariae was measured.
ColCAT3.6 contains 3.6 kb (positions -3521 to +115) of the rat COL1A1 gene
ligated to the chloramphenicol acetyltransferase (CAT) reporter gene.
ColCAT2.3 and ColCAT1.7 are 5' deletion mutants which contain 2,296 and
1,672 bp, respectively, of COL1A1 DNA upstream from the transcription
start site. ColCAT3.6 activity was 4- to 6-fold lower in primary
bone ***cell*** cultures than in intact calvariae, while
ColCAT2.3 activity was at least 100-fold lower in primary ***bone***
cells than in calvariae. These changes were accompanied by a

threefold decrease in collagen synthesis and COL1A1 mRNA levels in primary
bone ***cells*** compared with collagen synthesis and COL1A1
mRNA levels in freshly isolated calvariae. ColCAT3.6 and ColCAT2.3
activity was maintained in calvariae cultured in the presence or absence
of serum for 4 to 7 days. Thus, when ***bone*** ***cells*** are
removed from their normal microenvironment, there is parallel
downregulation of collagen synthesis, collagen mRNA levels, and ColCAT3.6
activity, with a much greater decrease in ColCAT2.3. These data suggest
that a 624-bp region of the ***COL1A1*** ***promoter*** between
positions -2296 and -1672 is active in intact and cultured bone but
inactive in cultured cells derived from the bone. We suggest that the
downregulation of COL1A1 activity in primary ***bone*** ***cells***
may be due to the loss of cell shape or to alterations in cell-cell and/or
cell-matrix interactions that normally occur in intact bone.

L60 ANSWER 8 OF 8 MEDLINE DUPLICATE 7
AN 92112960 MEDLINE
DN 92112960
TI Differential utilization of regulatory domains within the alpha 1(I)
collagen promoter in osseous and fibroblastic cells.
AU Pavlin D; Lichtler A C; Bedalov A; Kream B E; Harrison J R; Thomas H F;
Gronowicz G A; Clark S H; Woody C O; Rowe D W
CS Department of Pediatrics, University of Connecticut Health Center,
Farmington 06032.
NC AR38933 (NIAMS)
AR39850 (NIAMS)
1 KM DE00239 (NIDR)
SO JOURNAL OF CELL BIOLOGY, (1992 Jan) 116 (1) 227-36.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199204
AB Type I collagen is expressed in a variety of connective tissue cells and
its transcriptional regulation is highly complex because of the influence
of numerous developmental, environmental, and hormonal factors. To
investigate the molecular basis for one aspect of this complex regulation,
the expression of alpha 1(I) collagen (COL1A1) gene in osseous tissues, we
fused a 3.6-kb DNA fragment between bases -3,521 and +115 of the rat
COL1A1 ***promoter*** , and three deletion mutants, to the
chloramphenicol acetyltransferase (CAT) marker gene. The expression of
these ColCAT transgenes was measured in stably transfected osteoblastic
cell lines ROS 17/2.8, Py-1a, and MC3T3-E1 and three fibroblastic lines
NIH-3T3, Rat-1, and EL2. Deletion of the distal 1.2-kb fragment of the
full-length ColCAT 3.6 construct reduced the promoter activity 7- to
30-fold in the osteoblastic cell lines, twofold in EL2 and had no effect
in NIH-3T3 and Rat-1 cells. To begin to assess the function of COL1A1
upstream regulatory elements in intact animals, we established transgenic
mouse lines and examined the activity of the ColCAT3.6 construct in
various tissues of newborn animals. The expression of this construct
followed the expected distribution between the high and low
collagen-producing tissues: high levels of CAT activity in calvarial bone,
tooth, and tendon, a low level in skin, and no detectable activity in
liver and brain. Furthermore, CAT activity in calvarial bone was three- to
fourfold higher than that in the adjacent periosteal layer. Immunostaining
for CAT protein in calvaria and developing tooth germ of ColCAT3.6 mice
also confirmed the preferred expression of the transgene in differentiated
osteoblasts and odontoblasts compared to fibroblast-like cells of
periosteum and dental papilla. This study suggests that the 3.6-kb DNA
fragment confers the strong expression of COL1A1 gene in high collagen
producing tissues of intact animals and that the 5' flanking promoter
sequence between -3,521 and -2,295 bp contains one or more stimulatory
elements which are preferentially active in osteoblastic cells.

=> s col2a1/ab,bi
'AB' IS NOT A VALID FIELD CODE
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'AB' IS NOT A VALID FIELD CODE
L61 893 COL2A1/AB,BI

=> s col2a1 promoter/ab,bi
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
'AB' IS NOT A VALID FIELD CODE
L62 24 COL2A1 PROMOTER/AB,BI

=> dup rem l62
PROCESSING COMPLETED FOR L62
L63 12 DUP REM L62 (12 DUPLICATES REMOVED)

=> d 1- bib ab
YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

L63 ANSWER 1 OF 12 CAPLUS COPYRIGHT 1999 ACS
AN 1999:445332 CAPLUS
DN 131:69064
TI A functional analysis of the ***COL2A1*** ***promoter*** : the
transcription factor delta-EF1 is involved in E2 box-mediated repression
of COL2A1 gene transcription
AU Murray, Darryl Maurice
CS Johns Hopkins Univ., Baltimore, MD, USA
SO (1999) 85 pp. Avail.: UMI, Order No. DA9920766
From: Diss. Abstr. Int., B 1999, 60(2), 499
DT Dissertation
LA English
AB Unavailable

L63 ANSWER 2 OF 12 MEDLINE DUPLICATE 1
AN 1999296490 MEDLINE
DN 99296490
TI SV40 large T antigen expression driven by col2a1 regulatory sequences
immortalizes articular chondrocytes but does not allow stabilization of
type II collagen expression.
AU Steimberg N; Viengchareun S; Biehlmann F; Guenal I; Mignotte B; Adolphe M;
Thenet S
CS Ecole Pratique des Hautes Etudes, Laboratoire de Pharmacologie Cellulaire,
Centre de Recherches Biomedicales des Cordeliers, 15 rue de l'Ecole de
Medecine, Paris, 75006, France.
SO EXPERIMENTAL CELL RESEARCH, (1999 Jun 15) 249 (2) 248-59.
Journal code: EPB. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199909
EW 19990902
AB Immortalization of chondrocytes by SV40 T Ag has often been reported to

trigger the loss of expression of type II collagen, one of the main differentiation markers, although some immortalized chondrocyte lines maintaining a differentiated phenotype have also been described. Here, we show using transient cotransfections in differentiated chondrocytes that, in contrast to c-src, neither SV40 T Ag, nor c-myc, decreases col2a1 transcriptional activity. Then, we report the possibility of immortalizing rabbit articular chondrocytes by expression of SV40 T Ag controlled by the ***col2a1*** ***promoter*** and enhancer (pCol2SV). This strategy allows one to select within a population of differentiated chondrocytes those which are able to maintain functional regulation of the col2a1 gene through long-term culture. In precrisis pCol2SV-transfected chondrocytes, all-trans-retinoic acid, a down-regulator of col2a1 expression, induced apoptosis, strongly suggesting the strict control of T Ag expression by col2a1 regulatory sequences. Some pCol2SV-transfected chondrocytes were definitively immortalized, after a short crisis period. However, type II collagen synthesis was restricted to a small proportion of cells, which went on to decrease with subculture, while the proportion of cells expressing T Ag was not affected. In these postcrisis cells, T Ag remained at least partially under the control of functional col2a1 regulatory elements as assessed by all-trans-retinoic acid down-regulation. Copyright 1999 Academic Press.

L63 ANSWER 3 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:468445 BIOSIS
DN PREV199800468445
TI Stimulation of Sp1 DNA binding activity recognizing the human type II procollagen gene (***COL2A1***) ***promoter*** by tumor necrosis factor alpha(TNFalpha) in cultured human chondrocytes.
AU Liu, Gang; Dharmavaram, Rita; Jimenez, Sergio
CS Div. Rheumatology, Jefferson Med. Coll., Thomas Jefferson Univ., Philadelphia, PA 19107 USA
SO Arthritis & Rheumatism, (Sept., 1998) Vol. 41, No. 9 SUPPL., pp. S43.
Meeting Info.: 62nd National Scientific Meeting of the American College of Rheumatology and the 33rd National Scientific Meeting of the Association of Rheumatology Health Professionals San Diego, California, USA November 8-12, 1998 American College of Rheumatology
. ISSN: 0004-3591.
DT Conference
LA English

L63 ANSWER 4 OF 12 MEDLINE DUPLICATE 2
AN 1998001661 MEDLINE
DN 98001661
TI Detection and characterization of Sp1 binding activity in human chondrocytes and its alterations during chondrocyte dedifferentiation.
AU Dharmavaram R M; Liu G; Mowers S D; Jimenez S A
CS Division of Rheumatology, Department of Medicine, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.
NC AR39740 (NIAMS)
AR07583 (NIAMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Oct 24) 272 (43) 26918-25.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199802
EW 19980204
AB We have detected DNA binding activity for a synthetic oligonucleotide containing an Sp1 consensus sequence in nuclear extracts from human chondrocytes. Changes in the levels of Sp1 oligonucleotide binding activity were examined in nuclear extracts from freshly isolated human chondrocytes, from chondrocytes that had been cultured under conditions that allowed the maintenance of a chondrocyte-specific phenotype on plastic dishes coated with the hydrogel poly(2-hydroxyethyl methacrylate), and from chondrocytes induced to dedifferentiate into fibroblast-like cells by passage in monolayer culture on plastic substrata. It was observed that Sp1 binding was 2-3-fold greater in nuclear extracts from dedifferentiated chondrocytes than in nuclear extracts from either freshly isolated chondrocytes or from cells cultured in suspension. The Sp1 binding activity was specific, since it was competed by unlabeled Sp1 but not by AP1 or AP2. The addition of a polyclonal antibody against Sp1 to nuclear extracts from freshly isolated chondrocytes or to extracts isolated from chondrocytes cultured in monolayer decreased the binding of Sp1 by approximately 85%. However, when the same experiment was carried out with nuclear extracts prepared from cells cultured on poly(2-hydroxyethyl methacrylate)-coated plates, only a very slight inhibition of Sp1 binding was observed. When fragments of the ***COL2A1*** ***promoter*** containing putative Sp1 binding sites amplified by polymerase chain reaction were examined, it was found that the amounts of DNA-protein complex formed with nuclear extracts from dedifferentiated chondrocytes were 2-3-fold greater than the amounts formed with nuclear extracts from freshly isolated chondrocytes or from cells cultured in suspension. Quantitation of DNA binding activity by titration experiments demonstrated that nuclear extracts from fibroblast-like cells contained approximately 2-fold greater Sp-1 specific binding activity than nuclear extracts from chondrocytes. The direct role of Sp1 in type II collagen gene transcription was demonstrated by co-transfection experiments of ***COL2A1*** ***promoter*** -CAT constructs in Drosophila Schneider line L2 cells that lack Sp1 homologs. This is the first demonstration of Sp1 binding activity in human chondrocytes and of differences in Sp1 DNA binding activity between differentiated and dedifferentiated chondrocytes.

L63 ANSWER 5 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1998:157507 BIOSIS
DN PREV199800157507
TI Regulation of type II procollagen gene (***COL2A1***) ***promoter*** by transcription factor SP1 and quantitation of alterations in SP1 binding activity in normal human chondrocytes and during chondrocyte dedifferentiation.
AU Dharmavaram, Rita M.; Liu, Gang; Jimenez, Sergio A.
CS Dep. Med., Rheumatol. Div., Thomas Jefferson Univ., Philadelphia, PA 19107 USA
SO Arthritis & Rheumatism, (Sept., 1997) Vol. 40, No. 9 SUPPL., pp. S127.
Meeting Info.: 61st National Scientific Meeting of the American College of Rheumatology and the 32nd National Scientific Meeting of the Association of Rheumatology Health Professionals Washington, DC, USA November 8-12, 1997 Association of Rheumatology Health Professionals
. ISSN: 0004-3591.

DT Conference
LA English

L63 ANSWER 6 OF 12 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:97903 BIOSIS
DN PREV199799397106
TI Minimal cis-acting elements for chondrocyte-specific expression of the
mouse pro-alpha-1(II) collagen gene in transgenic mice.
AU Zhou, Guang; Lefebvre, Veronique; Mukhopadhyay, Krish; Smith, Chad; Zhang,
Zhaoping; Eberspaecher, Heidi; Garofalo, Silvio; De Crombrugghe, Benoit
CS Dep. Mol. Genet., Univ. Texas, M.D. Anderson Cancer Cent., Houston, TX
77030 USA
SO Molecular Biology of the Cell, (1996) Vol. 7, No. SUPPL., pp. 620A.
Meeting Info.: Annual Meeting of the 6th International Congress on Cell
Biology and the 36th American Society for Cell Biology San Francisco,
California, USA December 7-11, 1996
ISSN: 1059-1524.
DT Conference; Abstract; Conference
LA English

L63 ANSWER 7 OF 12 CAPLUS COPYRIGHT 1999 ACS
AN 1996:482269 CAPLUS
DN 125:134714
TI A 47-bp sequence of the first intron of the mouse pro.alpha.1(II) collagen
gene is sufficient to direct chondrocyte expression
AU Lefebvre, Veronique; Mukhopadhyay, Krish; Zhou, Guang; Garofalo, Silvio;
Smith, Chad; Eberspaecher, Heidi; Kimura, James H.; de Crombrugghe, Benoit
CS M. D. Anderson Cancer Center, University Texas, Houston, TX, 77030, USA
SO Ann. N. Y. Acad. Sci. (1996), 785(Molecular and Developmental Biology of
Cartilage), 284-287
CODEN: ANYAA9; ISSN: 0077-8923
DT Journal
LA English
AB Promoter deletion anal. showed that a 47-bp sequence of the Col2a1 gene
1st intron contains cis-acting sequences that are sufficient for promoter
activation in chondrocytes and that the ***Col2a1*** ***promoter***
does not contain sequences necessary for chondrocyte expression.

L63 ANSWER 8 OF 12 MEDLINE DUPLICATE 3
AN 96070901 MEDLINE
DN 96070901
TI Use of a new rat chondrosarcoma cell line to delineate a 119-base pair
chondrocyte-specific enhancer element and to define active promoter
segments in the mouse pro-alpha 1(II) collagen gene.
AU Mukhopadhyay K; Lefebvre V; Zhou G; Garofalo S; Kimura J H; de Crombrugghe
B
CS Department of Molecular Genetics, University of Texas, M. D. Anderson
Cancer Center, Houston 77030, USA.
NC AR 40335 (NIAMS)
AR 42909 (NIAMS)
CA16672 (NCI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Nov 17) 270 (46) 27711-9.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199603
AB We show that a new rat chondrosarcoma (RCS) cell line established in
long-term culture from the Swarm tumor displayed a stable differentiated
chondrocyte-like phenotype. Indeed, these cells produced the collagen
types II, IX, and XI and alcian blue-stainable cartilage-specific
proteoglycans, but no type I or type III collagen. To functionally
characterize their chondrocytic nature, the cells were stably transfected
with a type II collagen/beta geo chimeric gene which confers essentially
perfect chondrocyte-specific expression in transgenic mice. RCS cells
expressed both beta-galactosidase and G418 resistance, in comparison with
similarly transfected 10T1/2 and NIH/3T3 fibroblasts which did not. These
cells were then used to perform a systematic deletion analysis of the
first intron of the mouse type II collagen gene (Col2a1) using transient
expression experiments to determine which segments stimulated expression
of a luciferase reporter gene in RCS cells but not in 10T1/2 fibroblasts.
Cloning of two tandem copies of a 156-base pair (bp) intron 1 fragment
(+2188 to +2343) in a construction containing a 314-bp ***Col2a1***
promoter caused an almost 200-fold increase in promoter activity
in RCS cells but no increase in 10T1/2 cells. DNase I footprint analysis
over this 156-bp fragment revealed two adjacent protected regions, FP1 and
FP2, located in the 3'-half of this segment, but no differences were seen
with nuclear extracts of RCS cells and 10T1/2 fibroblasts. Deletion of FP2
to leave a 119-bp segment decreased enhancer activity by severalfold, but
RCS cell specificity was maintained. Further deletions indicated that
sequences both in the 5' part of the 119-bp fragment and in FP1 were
needed simultaneously for RCS cell-specific enhancer activity. A series of
deletions in the promoter region of the mouse Col2a1 gene progressively
reduced activity when these promoters were tested by themselves in
transient expression experiments. However, these promoter deletions were
all activated to a similar level in RCS cells by a 231-bp intron 1
fragment that included the 156-bp enhancer. The RCS cell-specific activity
persisted even if the ***Col2a1*** ***promoter*** was replaced by
a minimal adenovirus major late promoter. This 231-bp intron 1 fragment
also had strong enhancing activity in transiently transfected mouse
primary chondrocytes. Our experiments establish the usefulness of RCS
cells as an experimental system for studies of the control of
chondrocyte-specific genes, provide an extensive delineation of segments
in the Col2a1 first intron involved in chondrocyte-specific activity, and
show that promoter sequences are dispensable for chondrocyte specificity.

L63 ANSWER 9 OF 12 MEDLINE DUPLICATE 4
AN 96360245 MEDLINE
DN 96360245
TI A 182 bp fragment of the mouse pro alpha 1(II) collagen gene is sufficient
to direct chondrocyte expression in transgenic mice.
AU Zhou G; Garofalo S; Mukhopadhyay K; Lefebvre V; Smith C N; Eberspaecher H;
de Crombrugghe B
CS Department of Molecular Genetics, University of Texas, M. D. Anderson
Cancer Center, Houston 77030, USA.
NC AR 40335 (NIAMS)
AR 42909 (NIAMS)
SO JOURNAL OF CELL SCIENCE, (1995 Dec) 108 (Pt 12) 3677-84.
Journal code: HNK. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199705
EW 19970502
AB Type II collagen is a major chondrocyte-specific component of the
cartilage extracellular matrix and it represents a typical differentiation
marker of mature chondrocytes. In order to delineate cis-acting elements
of the mouse pro alpha 1(II) collagen gene that control
chondrocyte-specific expression in intact mouse embryos, we generated
transgenic mice harboring chimeric constructions in which varying lengths
of the promoter and intron 1 sequences were linked to a beta-galactosidase
reporter gene. A construction containing a 3,000 bp promoter and a 3,020
bp intron 1 fragment directed high levels of beta-galactosidase expression
specifically to chondrocytes. Expression of the transgene coincided with
the temporal expression of the endogenous gene at all stages of embryonic
development. Successive deletions of intron 1 delineated a 182 bp fragment
which targeted beta-galactosidase expression to chondrocytes with the same
specificity as the larger intron 1 fragment. Transgenic mice harboring a
309 bp ***Col2a1*** ***promoter*** lacking intron 1 tester
sequences showed no beta-galactosidase expression in chondrocytes.
Reduction of the 182 bp fragment to a 73 bp subfragment surrounding a
decamer sequence previously reported to be involved in chondrocyte
specificity, resulted in loss of transgene expression in chondrocytes.
When the ***Col2a1*** ***promoter*** was replaced with a minimal
beta-globin promoter, the 182 bp intron 1 sequence was still able to
target expression of the transgene to chondrocytes. We conclude that a 182
bp intron 1 DNA segment of the mouse Col2a1 gene contains the necessary
information to confer high-level, temporally correct, chondrocyte
expression on a reporter gene in intact mouse embryos and that
Col2a1 ***promoter*** sequences are dispensable for
chondrocyte expression.

L63 ANSWER 10 OF 12 MEDLINE DUPLICATE 5
AN 94175898 MEDLINE
DN 94175898
TI Synthesis of recombinant human procollagen II in a stably transfected
tumour cell line (HT1080).
AU Fertala A; Sieron A L; Ganguly A; Li S W; Ala-Kokko L; Anumula K R;
Prockop D J
CS Department of Biochemistry and Molecular Biology, Jefferson Institute of
Molecular Medicine, Jefferson Medical College, Thomas Jefferson
University, Philadelphia, PA 19107.
NC AR38188 (NIAMS)
SO BIOCHEMICAL JOURNAL, (1994 Feb 15) 298 (Pt 1) 31-7.
Journal code: 9YO. ISSN: 0264-6021.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199406
AB Apparently because the biosynthetic pathways involve eight or more highly
specific post-translational enzymes, it has been difficult to obtain
expression of genes for fibrillar collagens in recombinant systems. Here
two constructs of the human gene for procollagen II (COL2A1) were
prepared, one with about 0.5 kb of a promoter for a procollagen I gene
(COL1A1) and the other with about 4 kb of the promoter for the procollagen
II gene. The constructs, together with a neomycin-resistant gene, were
transfected into a human tumour cell line (HT1080) that synthesizes the
collagen IV found in basement membranes, but does not synthesize any
fibrillar collagen. About two per 100 clones resistant to the neomycin
analogue G418 synthesized and secreted human procollagen II. Milligram
quantities of the recombinant procollagen II were readily isolated from
the cultured medium. The recombinant procollagen II had the expected amino
acid sequence as defined by nucleotide sequencing of mRNA-derived cDNA and
the expected amino acid composition as defined by analysis of procollagen
II that was converted into collagen II by digestion with procollagen N-
and C-proteinases. Also, analysis of the carbohydrate content indicated
that there was glycosylation of some of the hydroxylysine residues but no
evidence of post-translational overmodification of the residues. In
addition, the protein was shown to have a native conformation as assayed
by a series of protease digestions. No essential differences were found
between clones transfected with the COL2A1 gene construct containing the
COL1A1 promoter and the similar construct containing the
COL2A1
promoter in terms of number of clones synthesizing recombinant
procollagen II and the levels of expression. With both constructs, the
expression of the COL2A1 gene was closely related to copy number. The
results demonstrated therefore that it is not essential to use a promoter
for a gene normally expressed in a host cell in order to obtain gene
copy-number-dependent expression of an exogenous collagen gene in stably
transfected cells.

L63 ANSWER 11 OF 12 CAPLUS COPYRIGHT 1999 ACS
AN 1994:185638 CAPLUS
DN 120:185638
TI Synthesis of recombinant human procollagen II in a stably transfected
tumor cell line (HT1080)
AU Fertala, Andrzej; Sieron, Aleksander L.; Ganguly, Arupa; Li, Shi-Wu;
Ala-Kokko, Leena; Anumula, Kalyan R.; Prockop, Darwin J.
CS Jefferson Med. Coll., Thomas Jefferson Univ., Philadelphia, PA, 19107, USA
SO Biochem. J. (1994), 298(1), 31-7
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
AB Apparently because the biosynthetic pathways involve eight or more highly
specific post-translational enzymes, it has been difficult to obtain
expression of genes for fibrillar collagens in recombinant systems. Here
two constructs of the human gene for procollagen II (COL2A1) were prepd.,
one with about 0.5 kb of a promoter for a procollagen I gene (COL1A1) and
the other with about 4 kb of the promoter for the procollagen II gene.
The constructs, together with a neomycin-resistant gene, were transfected
into a human tumor cell line (HT1080) that synthesizes the collagen IV
found in basement membranes, but does not synthesize any fibrillar
collagen. About two per 100 clones resistant to the neomycin analog G418
synthesized and secreted human procollagen II. Milligram quantities of
the recombinant procollagen II were readily isolated from the cultured
medium. The recombinant procollagen II had the expected amino acid
sequence as defined by nucleotide sequencing of mRNA-derived

cDNA and the
expected amino acid compn. as defined by anal. of procollagen II that was
converted into collagen II by digestion with procollagen N- and C-proteinases. Also, anal. of the carbohydrate content indicated that
there was glycosylation of some of the hydroxylysine residues but no
evidence of post-translational overmodification of the residues. In addn., the protein was shown to have a native conformation as assayed by a
series of protease digestions. No essential differences were found between clones transfected with the COl2A1 gene construct contg. the
COL1A1 promoter and the similar construct contg. the ***COL2A1***
promoter in terms of no. of clones synthesizing recombinant
procollagen II and the levels of expression. With both constructs, the
expression of the COL2A1 gene was closely related to copy no. The results
demonstrated therefore that it is not essential to use a promoter for a
gene normally expressed in a host cell in order to obtain gene copy-no.-dependent expression of an exogenous collagen gene in stably
transfected cells.

L63 ANSWER 12 OF 12 CAPLUS COPYRIGHT 1999 ACS
AN 1993:464289 CAPLUS
DN 119:64289
TI Structural analysis of the regulatory elements of the type-II procollagen
gene. Conservation of promoter and first intron sequences between human
and mouse
AU Vikkula, Miikka; Metsaranta, Marjo; Syvanen, Ann Christine; Ala-Kokko,
Leena; Vuorio, Eero; Peltonen, Leena
CS Dep. Hum. Mol. Genet., Natl. Public Health Inst., Helsinki, Finland
SO Biochem. J. (1992), 285(1), 287-94
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
AB Transcription of the type-II procollagen gene (COL2A1) is very specifically restricted to a limited no. of tissues, particularly
cartilages. Transcription of the type-II procollagen gene (COL2A1) is
very specifically restricted to a limited no. of tissues, particularly
cartilages. In order to identify transcription-control motifs, the promoter region and the first intron of the human and mouse COL2A1 genes
were sequenced. In order to identify transcription-control motifs, the
promoter region and the first intron of the human and mouse COL2A1 genes
were sequenced. With the assumption that these motifs should be well
conserved during evolution, a search was made for potential elements
important for the tissue-specific transcription of the COL2A1 gene by
aligning the 2 sequences with each other and with the available rat type-II procollagen sequence for the promoter. With the assumption that
these motifs should be well conserved during evolution, a search was made
for potential elements important for the tissue-specific transcription of
the COL2A1 gene by aligning the 2 sequences with each other and with the
available rat type-II procollagen sequence for the promoter. Specific
evolutionarily well-conserved motifs in the promoter area were identified.
Specific evolutionarily well-conserved motifs in the promoter area were
identified. However, several suggested regulatory elements in the promoter region did not show evolutionary conservation. However, several
suggested regulatory elements in the promoter region did not show evolutionary conservation. In the middle of the first intron was a
cluster of well-conserved transcription-control elements; these conserved
motifs most probably possess a significant function in the control of the
tissue-specific transcription of the COL2A1 gene. In the middle of the
first intron was a cluster of well-conserved transcription-control elements; these conserved motifs most probably possess a significant
function in the control of the tissue-specific transcription of the COL2A1
gene. Locations of addnl., highly conserved nucleotide stretches were
identified which are good candidate regions in the search for binding
sites of yet-uncharacterized cartilage-specific transcription regulators
of the COL2A1 gene. Locations of addnl., highly conserved nucleotide
stretches were identified which are good candidate regions in the search
for binding sites of yet-uncharacterized cartilage-specific transcription
regulators of the COL2A1 gene.

=> d his

(FILE 'HOME' ENTERED AT 15:12:44 ON 18 OCT 1999)

FILE 'MEDLINE' ENTERED AT 15:12:49 ON 18 OCT 1999
L1 142 S STROMA#(P)(EXOGENOUS GENE OR GENE CONSTRUCT OR VECTOR)/AB,BI
L2 26 S L1 AND PROMOTER#/AB,BI
L3 1 S L2 AND COLLAGEN/AB,BI
L4 14675 S MESENCHYM?/AB,BI
L5 64 S L4(P)(GENE CONSTRUCT OR EXOGENOUS GENE OR VECTOR#)/AB,BI
L6 12 S L5 AND PROMOTER#/AB,BI
L7 443 S STROMAL FIBROBLAST#/AB,BI
L8 11 S L7(P)(VECTOR# OR CONSTRUCT#)/AB,BI
L9 398 S OBESITY GENE OR OBESITY PROTEIN OR OB GENE/AB,BI
L10 1 S L9(10A)(CONSTRUCT OR VECTOR)/AB,BI
L11 0 S OB GENE AND (MESENCHYMAL OR MARROW STROMA# OR STROMAL FIBROBL
L12 69 S LTMC#
L13 0 S L12 AND OB GENE/AB,BI
L14 0 S L12 AND OBESITY FACTOR/AB,BI
L15 9 S OBESITY FACTOR/AB,BI
L16 1867 S LEPTIN/AB,BI
L17 385 S L16 AND ADIPOCYTE#/AB,BI
L18 8138 S ADIPOCYTE#/AB,BI
L19 54 S L18(10A)(CONSTRUCT OR EXOGENOUS OR VECTOR)/AB,BI
L20 1 S L19 AND (OB GENE OR LEPTIN)/AB,BI
L21 14812 S L1 OR L4
L22 0 S L21 AND (OB GENE OR LEPTIN)/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 15:28:51 ON 18
OCT 1999
L23 2 S L22
L24 2 DUP REM L23 (0 DUPLICATES REMOVED)
L25 9655 S OBESITY PROTEIN OR OBESITY FACTOR OR OBESITY GENE OR OB GENE
L26 1681 S L25 AND (STROMA# OR MESENCHYMAL OR ADIPOCYTE#)/AB,BI
L27 363 S L25 AND (CONSTRUCT# OR VECTOR# OR EXOGENOUS)/AB,BI
L28 79 S L27 AND (STROMA# OR MESENCHYMAL OR ADIPOCYTE#)/AB,BI
L29 35 DUP REM L28 (44 DUPLICATES REMOVED)
E PROCKOP DARWIN J/AU
L30 553 S E3-E4
L31 18 S L30 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
L32 12 DUP REM L31 (6 DUPLICATES REMOVED)
L33 0 S L32 AND PROMOTER#/AB,BI
E PEREIRA RUTH F/AU
L34 26 S E2-E4
L35 20 DUP REM L34 (6 DUPLICATES REMOVED)
L36 3 S L35 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
L37 3 DUP REM L36 (0 DUPLICATES REMOVED)
E LEEPER DENNIS B/AU
L38 40 S E2-E3

L39 2 S L38 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
L40 1 DUP REM L39 (1 DUPLICATE REMOVED)
E OHARA MICHAEL D/AU
E KULKOSKY JOSEPH/AU
L41 79 S E1-E5
L42 0 S L41 AND (MARROW STROMA# OR MESENCHYMAL)/AB,BI
E PHINNEY DONALD/AU
L43 26 S E3-E5
L44 7 S L43 AND (STROMA# OR MESENCHYMAL)/AB,BI
L45 6 DUP REM L44 (1 DUPLICATE REMOVED)
E LAPTEV ALEXEY/AU
L46 15 S E1-E4
L47 5 S L46 AND (STROMA# OR MESENCHYMAL)/AB,BI
L48 4 DUP REM L47 (1 DUPLICATE REMOVED)
L49 163 S (STROMA#)(10A)(PROMOTER#)/AB,BI
L50 4 S L49(10A)(COLLAGEN)/AB,BI
L51 1 DUP REM L50 (3 DUPLICATES REMOVED)
L52 0 S L49(10A)(PROCOLLAGEN OR COL1A1 OR COL2A1)/AB,BI
L53 200 S (PROCOLLAGEN OR COL1A1 OR COL2A1)(W)(PROMOTER#)/AB,BI
L54 0 S L53(P)(OBESITY GENE OR OB GENE OR OBESITY PROTEIN OR LEPTIN)
L55 0 S L53(10A)(STROMA# OR MESENCHYMAL)/AB,BI
L56 0 S L53(10A)(MARROW)/AB,BI
L57 4 S L53(P)(STROMA# OR MESENCHYMAL)/AB,BI
L58 1 DUP REM L57 (3 DUPLICATES REMOVED)
L59 29 S L53(P)(BONE CELL# OR OSTEOBLAST# OR PREOSTEOBLAST#)/AB,BI
L60 8 DUP REM L59 (21 DUPLICATES REMOVED)
L61 893 S COL2A1/AB,BI
L62 24 S COL2A1 PROMOTER/AB,BI
L63 12 DUP REM L62 (12 DUPLICATES REMOVED)

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 320.92 338.48

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE -10.71 -10.71

STN INTERNATIONAL LOGOFF AT 15:49:19 ON 18 OCT 1999

Host Name: +++
OK
ATHZ
OK